The Journal of Obstetrics and Gynæcology of the British Empire

Vol. IV. JULY, 1903. No. 1.

ON CHORIONEPITHELIOMA AND THE OCCURRENCE OF CHORIONEPITHELIOMATOUS AND HYDATIDIFORM MOLE-LIKE STRUCTURES IN TERATOMATA. A PATHOLOGICAL AND CLINICAL STUDY.*

By JOHN H. TEACHER, M.A., M.B.C.M., *Underkeeper in the Anatomical and Pathological Department of the Hunterian Museum in the University of Glasgow.*

PART I.

	Page.
1. Introduction	2
2. The History of Chorionepithelioma	7
3. The Physiological Prototype of Chorionepithelioma	18
4. Reports of the Cases	29
5. Histological Details	42
6. The Chorionepithelioma of Teratomata	52
7. Description of the Illustrations	60

* Thesis presented for the degree of M.D., University of Glasgow. An abstract was read to the Obstetrical Society of London on June 3rd, 1903.

129773

INTRODUCTION.

ALTHOUGH it is only 14 years since the recognition of deciduoma malignum as a special disease, the literature of the subject is already very large. There is, perhaps, no tumour which has given rise to so much discussion or to so many divergent views as to its origin and nature. Within the last four or five years, however, we seem to have attained a considerable degree of certainty on these points.

On looking into the literature of the disease I found that, whatever might be the state of opinion regarding its pathology on the Continent, in this country it was far from unanimous, and the most constant stumbling block appeared to be the decision of the Obstetrical Society of London, as the outcome of the discussion which they held in the year 1896, that these tumours were only sarcomata of the uterus. From the accounts given not only in obstetrical and gynæcological text-books, but also in special works on tumours, and in the reports of cases of deciduoma malignum in the journals, it was apparent that in England, at any rate, this opinion was still the cause of much confusion. Some even questioned the existence of such tumours. On the other hand, all who have reported cases in Scotland have followed the view of the disease which is associated with the name of Marchand, and recently that opinion has also won many adherents in England.

In 1898, along with Dr. J. K. Kelly, I reported the first case of the kind observed in Scotland.† After an interval of four years I took up the subject again with the view of reporting a new case which had been put into my hands for examination in October, 1901. Shortly afterwards another case (case iii.) in which the difficulties of the diagnosis of this disease are illustrated was handed over to me, and about a year later a third case (case ii.) very similar to the first.

†"A Case of Deciduoma Malignum," by J. K. Kelly, M.D., and John H. Teacher, M.A., M.B., C.M., *Journ. of Path. and Bact*, October, 1898, p. 358.

Having regard to the amount of importance still attached to the discussion in the Obstetrical Society of London, and the fact that in spite of the great advances in our knowledge, no more recent thorough discussion has been held by the Society, I approached them last September with a request that they would allow me to communicate these cases to them. At this time I was just starting on a visit to the German Schools of Medicine, and what I saw and heard there, confirmed me in my opinion that it would be well worth while to write a new English review of the whole subject. In Austria and Germany I had the privilege of studying many of the classic cases and also most of the best material relating to the development and structure of the placenta, with which deciduoma malignum is so closely bound up.

On the Continent I found that though any case of deciduoma malignum was an object of considerable interest, it was not on account of the problem as to its nature or origin; this is regarded as settled by the demonstration in numerous cases of the actual development of the growth out of the epithelium of the chorionic villi. Further the nature of the epithelium also seems to be fairly well determined, and with it the question of the classification of the tumour. The name "deciduoma malignum" is still often used, but the view implied by it is completely abandoned in favour of that of Marchand expressed in the term "chorionepithelioma." I also heard a good deal of comment on what was called the "English opinion," meaning that of the Obstetrical Society of London.

In September, 1902, I attended the Versammlung Deutscher Naturforscher und Aerzte in Carlsbad, and became acquainted with certain recent discoveries which had greatly increased the interest felt in the subject. These were contained in a paper published in May, 1902, by Friedrich Schlagenhaufer, of Vienna. He described two cases of malignant tumour of the testis, in which were found structures identical, histologically and in their behaviour to the adjacent tissues, with chorionepithelioma; while, in one of them, structures closely resembling hydatidiform mole were present, which had spread from the testicular tumour into the veins and even into the cavities of the heart. Schlagenhaufer's cases formed the subject of a lively discussion in the pathological section of the congress, and I have since then had the pleasure of meeting him in Vienna and examining his material in detail. His conclusion that the tumours were teratomata was very generally accepted as valid. These tumours are of great interest in themselves, but they have also a special interest, for in them apparently we meet again the "sarcoma

of the testis," which was shown to the Committee of the Obstetrical Society of London by the late Professor Kanthack and Dr. Eden, which provided one of the reasons on which the decision of the Society was founded.

The practical importance of chorionepithelioma is shown by the number of cases that have been reported since it was recognized. A considerable number certainly are cases which had previously been recorded under other names, but, after excluding these, there are more than sufficient to show that it is by no means the great rarity that it was supposed to be. After rejecting a number which appeared doubtful, I have been able to tabulate from the literature 188 well authenticated cases, of which I was also able to obtain the principal details. In addition to these, there are a good number of the ordinary cases of the disease lying unpublished, only the unusual ones being now recorded. By the kindness of Professor Weichselbaum, I obtained portions of the specimens which have been added to the museum of the General Hospital in Vienna between February, 1901, and August, 1902. Of these, seven in number, only two have been published. The rest were examined and then placed in the museum. All of them were fatal cases. In addition, I was informed that several others in the same period had been simply examined and thrown out as if they were ordinary cases of carcinoma of the cervix. The published cases are those of Hubl. Schlagenhaufer informed me that he had reported on six cases since 1897, but of these he had only published two. A like state of affairs, though perhaps not concerning so many cases, I encountered in Prague and Dresden; and in Kiel and Leipsic I saw sections of several new cases which are being worked up for publication.

In some parts of the world, it would appear from the above, chorionepithelioma is not an uncommon tumour. In the period of eighteen months above mentioned there would be, I was informed, about 2,700 post mortem examinations in connection with the General Hospital of Vienna; practically all patients who die there are examined by the pathologist. Even seven deaths in that number is no inconsiderable share for a disease which was supposed to be a rarity, and when one considers that most of the victims are women in the prime of life, and who have enjoyed good health up to the fatal pregnancy, the importance of the disease appears still greater. Although fewer cases have been reported from other countries, still the literature shows a considerable and rapidly increasing tale of them. One of the American cases, that of Williams, occurred in a negress. On the other hand, although the

pathologists of Budapest have been on the look-out for cases for several years, Dr. Krompecher informed me that there has not yet been found one in that city. It may be that it is almost equally rare in London. With a population more than twice that of Vienna, only some seven cases have been recorded. From other parts of England five cases, from Ireland one case, and from Scotland, including those here reported, nine cases have been put on record, and I am aware of one more which has been observed. Probably others have been dismissed as sarcomata and others have escaped notice through the rarity of post-mortem examinations in this country, passing for retained placenta and sepsis. A very suggestive story is that of a case recorded by Baldwin in the *American Journal of Obstetrics* of November, 1902.

> He was called to remove a cancer of the uterus, this being the diagnosis of the attending physician. He found the woman had been delivered at full term without difficulty six or eight weeks previous to his visit. The after-birth was delivered by itself, and so far as the attending physician knew, it was normal. Two weeks later, trouble continuing, another physician was sent for, who examined her, and found a piece of after-birth which he removed, curetted, and supposed there would be no further trouble. Criticism was indulged in, and a suit for malpractice was in the air. The second physician two or three weeks later, on examining the woman, found more after-birth. Dr. Baldwin again examined the woman carefully and found malignant disease, and told the physician it was deciduoma malignum. Vaginal hysterectomy was made. There was no involvement of the vagina. He was careful, however, to pull down the omentum, and found a secondary nodule as large as the end of his finger. Recovery was satisfactory, but a few weeks later the woman developed cachexia and died. He believed he had seen half a dozen such cases in his practice.

At the same time already evidence is not wanting that too hasty operations have been performed. The extreme malignancy of the earliest reported cases gave grounds for the opinion that operation could not be done too early, but the records of numerous cases more recently reported show that the extremely malignant disease is but one type and that there are all degrees of malignancy, just as in the other classes of tumour. The histological test has been proved to be by no means infallible, and neither clinically nor pathologically is it possible to draw a sharp line of distinction between the cases which are merely retained placenta and curable by removal of the foreign material, and those cases which run on into chorionepithelioma or destructive hydatidiform mole. It is especially with regard to the last mentioned variety of the tumour that difficulties are met.

The recognition of chorionic epithelium or chorionic villi is easy and certain, but to decide whether the villi are those of a simple hydatidiform mole or whether they are potential malignant growths is a very different matter.

Chorionepithelioma or deciduoma malignum may be defined generally as follows:—

It is a malignant tumour of the uterus arising in connection with a confinement or abortion which in typical cases destroys life with a rapidity almost unequalled by any other kind of growth. Clinically it is characterised by the occurrence within a shorter or longer period after the pregnancy of irregularly recurring hæmorrhages, progressive anæmia, and cachexia, sometimes fever and rigors. The morbid anatomy of the case shows a hæmorrhagic tumour situated most commonly in the cavity of the uterus, occupying the fundus and adjacent portions of the anterior and posterior wall of the body of the uterus, *i.e.*, the commonest site of the placenta. Other evidences of malignancy in addition to the violent hæmorrhages are more or less ulceration, infiltration, and destruction of the uterine tissues and the rapid occurrence of metastatic growths which are most common in the vaginal veins and the lungs, corresponding to a dissemination by the blood stream. Histologically it presents a very characteristic picture, but at the same time a complex and rather confusing one owing to the numerous modifications which the component cells undergo so that they present an extraordinary variety of forms.

The most typical elements are:—

(1) Small well defined polyhedral cells, with large vesicular nuclei closely packed together in masses without any connective tissue stroma between them.

(2) Large multi-nucleated irregular masses of protoplasm (plasmodia or synctia) in which no definite cell boundaries are recognizable.

(3) Large cells, sometimes mono-nucleated, sometimes multinucleated, some of which present a resemblance to decidua cells, while others are identical in character with the multi-nucleated giant cells which occur in the decidua serotina. These are, in some parts, arranged in cell masses without intervening tissue stroma, in other parts they are infiltrating and destroying adjacent tissues after the manner of sarcoma.

Among the cell masses are seen the remains of the normal tissues, and a large amount of blood, sometimes clotted, sometimes fluid, as

if in sinuses, giving the tissue its hæmorrhagic character. The tumour has no proper connective tissue stroma, or blood vessels of its own, nor does it convert the adjacent normal tissues into stroma. Instead, a particularly active destruction of them is characteristic, and specially it attacks and burrows into the uterine blood vessels. To this feature it owes its hæmorrhagic character and its mode of dissemination.

According to what may be called the accepted view, the connection with pregnancy is essential and the tumour is a quite peculiar growth originating from a structure peculiar to the gravid uterus, viz., the epithelium of the chorionic villi; the cells of the first class corresponding to the Langhans' layer; the second to the syncytium, and the third containing derivatives of both layers. Its place in a system of classification depends on the view that is held of the nature and source of that epithelium. The original view that it was a tumour composed of decidua cells is quite abandoned. The other views are the English one already mentioned, and what may be called the view of Veit. According to Veit the tumour is a sarcoma originating from uterine tissues while the fœtal elements, which he admits to be present, are non-essential and due to the superposition of a pregnancy on a primary maternal disease.

The History of Chorionepithelioma.

A very elaborate discussion of the history and literature of the deciduoma malignum has been rendered unnecessary by the publication of a very long and able *Zusammenfassendesreferat* by Max Münzer, in which practically all the cases that had been described up to the beginning of 1902, and all the opinions that have ever been held are most carefully, and, as I can vouch from my own reading, accurately epitomized and discussed. This, and the papers of Marchand for the details, contain certainly nearly all that anyone need read for a thorough knowledge of the general aspects of the subject. For the excentricities there are other monographs which will be referred to later. For those to whom German presents a difficulty, the older literature is very well presented in Whittridge William's paper of 1895, and the position in 1899 is summarized with exemplary brevity by Haultain. There are a number of other papers which give valuable information, among which may be mentioned those of McKenna, Gaylord, Fothergill, Berry-Hart, Ladinski, and Pierce.

The history of the deciduoma malignum considered as a special

disease begins with the description by Sänger in 1889 of a case of very malignant sarcoma-like growth of the body of the uterus, arising after an abortion in the eighth week. This he regarded not merely as a sarcoma coinciding with the pregnancy, but as a special tumour allied to the sarcomata in which pregnancy was an essential feature, *i.e.*, a growth developed from a tissue peculiar to the gravid uterus, viz.:—the decidua, and he called it deciduoma malignum. In 1890, Pfeiffer, a pupil of Chiari, published an account of a very peculiar case and classed along with it three cases which had been described in 1877 by Chiari as carcinoma of the uterus coinciding with pregnancy. Pfeiffer quite independently came to the same conclusion as Sänger, and also called the growth deciduoma malignum. From Italy, too, Pestalozza, in 1891, reported three cases of a highly malignant tumour of the uterus connected with pregnancy. One of these was a case of malignant hydatidiform mole. The whole three he described as *sarcoma hæmorrhagicum sen infectiousum*. Pestalozza recognised the importance of the pregnancy as giving to the tumour special characters, but he doubted the origin from decidua cells and regarded it as modified sarcoma of the uterus. Cases more or less similar to that of Sänger were also reported by Schmorl, Müller, Gottschalk, Lebensbaum, who did not, however, altogether accept Sänger's interpretation of the disease.

In 1893, Sänger published his monograph on the subject in which he collected all the earlier described tumours that seemed to present affinity to his case, and included also a number of old cases of destructive hydatidiform moles of which there had been no proper microscopic examination, and considered a number of other diseases of the placenta which had no direct connection with deciduoma and need not be further considered here. Sänger now divided the malignant tumours directly connected with pregnancy into three classes—

(1) Sarcoma deciduo-cellulare, *i.e.*, the sarcoma composed of decidua cells corresponding to the original deciduoma malignum. The name was altered to be more precise by excluding the glands of the decidua which played no part in the tumour.

(2) Sarcoma deciduo-cellulare with participation of chorionic villi. (*a*) After hydatidiform mole, (*b*) with a sarcomatous condition of the mesoblast of the villi (Schmorl's and Gottschalk's tumours.)

(3) The malignant interstitial hydatidiform moles and placental polypes.

The third class he held to be quite distinct from the decidual tumours; being a sort of parasitic growth of chorionic villi into the

maternal tissues which remained passive except for some inflammatory re-action. The second group formed the bridge between the real decidual tumours and the pure malignant moles. In the tumours he held that the decidua cells were the essential malignant elements, while the chorionic elements which had been described in Gottschalk's and one of Schmorl's cases were adventitious.

The views of Sänger as to the pathology of the condition have proved to be erroneous in many respects, but the great merit remains to him that he focussed the attention of gynæcologists and pathologists on the disease, and paved the way for a proper understanding of a condition, the practical importance of which has been indicated. Very soon it was proved that the tumour of which he may be said to be the discoverer, although not exactly common, was by no means a great rarity. Cases began to be reported in considerable numbers, many of them being old ones which had formerly been reported under different names.

Most of the cases were reported as deciduomata in the sense of Sänger, but divergent views also appeared, the number of which is indicated in the great number of names which were conferred upon the disease.* Gottschalk, in his complete publication in 1894, dissented from the view of Sänger and emphasized his view that the disease was one primarily of the fœtal tissues, being essentially a sarcoma of the chorion arising from the Langhans' layer (regarded by him as of fœtal mesoblastic nature), and the stroma of the villi. Schmorl also regarded the participation of fœtal tissues as essential to the tumour, but did not publish his views in detail. Menge, on the other hand, reported two cases taking the view that they were sarcomata originating from the uterine muscle. Cases were also reported as deciduomata in the sense of Sänger by Bacon, Tannen, Löhlein, Schauta, and others.

In 1895, L. Fränkel reported a case in which the growth consisted almost entirely of syncytium and called it syncytioma malignum or carcinoma syncytiale, because he regarded it as originating not from the decidua but from the syncytium of the chorionic epithelium. As to the exact nature of the syncytium he did not commit himself to an opinion. He also described the decidua-like infiltrating cells, but refrained from expressing a definite opinion as to their nature.

About the same time, Marchand published the papers which

*Gottschalk—sarcoma chorion-deciduo-cellulare; later sarcoma chorii; Schmorl—blastoma chorion-deciduo-cellulare; Pestalozza—sarcoma hæmorrhagicum sen infectiosum; Guttenplan—hæmorrhagic sarcoma; Meyer—epithelioma papillare uteri; Klebs—placental papilloma; Klien—deciduo-sarcoma uteri giganto-cellulare.

brought order out of this chaos. According to his view, the tumours were composed of cells derived from both layers of the chorionic epithelium; they were, therefore, accepting the ruling opinion as to the nature of that structure, of mixed maternal and fœtal origin. The difficulty of admitting that a tumour could be composed of fœtal and maternal tissues was fully met by the conception of the chorionic epithelium as so specialized a structure, and the symbiosis of these two elements as so characteristic and essential a physiological feature, that they were entitled to be considered together as if one tissue. It was on this ground as well as on the ground of their clinical history and histological structure—resemblances to both carcinoma and sarcoma—that Marchand regarded these growths as neither carcinoma nor sarcoma, but as *sui generis*. He suggested that they might be called serotinal tumours since they arose from tissues which occurred only in the region of the decidua serotina and the placenta.

Williams, of Johns Hopkins Hospital, in the same year, independently recognized the connection of deciduoma malignum with the chorionic epithelium, but, while recognizing elements resembling Langhans' layer cells, he considered the syncytium the important element. He was inclined to regard the latter as a derivative of the uterine epithelium and considered the fœtal epiblastic nature of the former a difficulty in the way of believing that the individual cells of the tumour could have this origin. He preferred to leave the question of their nature open.

The three last-mentioned authors then at least agreed in referring the tumour to the chorionic epithelium. As the particular view, however, which has prevailed is that of Marchand, the origin from the chorionic epithelium has come to be generally associated with his name. Indeed, it is to Marchand that the credit is chiefly due for unravelling the confusion in which the subject had become involved, and setting the pathology of it on a sure foundation of accurate observation and careful generalisation.

Marchand's theory of the nature and origin of the tumour was founded on a thorough investigation of the histology of the human placenta. He was able to trace a close resemblance—physiological and anatomical—between the chorion epithelium and the tissues composing the tumour. The frequency with which hydatidiform disease of the chorion precedes deciduoma had been noted and had been held by some observers to be no accident. In the study of hydatidiform mole in situ within the cavity of the uterus, Marchand demonstrated that the generally accepted view, that of Virchow, that

hydatidiform mole was a myxoma of the chorion was erroneous. The stroma of the villi is connective tissue, and in the young placenta it has the characters of embryonic connective or mucous tissue. Marchand found that the actual condition of this in the mole was dropsical degeneration. In the small vesicles (the early stage) there was much mucin, as was natural considering the nature of the tissue, but there was very little in the large vesicles, the contents being a watery fluid. Active proliferation of the mucous tissue there was none. The connective tissue was poor in nuclei and reduced to a thin rind beneath the epithelium. But there was excessive and irregular proliferation of both layers of the chorionic epithelium. This Marchand regarded as the important change. Later observers have, in the main, agreed with him. The condition may vary somewhat in different cases. There may be excessive proliferation as well as degeneration of the mesoblastic cores of the villi in some cases, but the important tissue with regard to tumour formation is the epithelium.

Besides setting the histology of the hydatidiform mole on a satisfactory basis, Marchand was able to trace an extremely close likeness between the hypertrophied epithelium in the mole and the cells composing deciduoma malignum. Not only were the cell forms which arose out of it the same, but they infiltrated the maternal tissues, and invaded the blood vessels in a similar way. This, he showed further, was but an exaggeration of the conditions found about the attachments of the villi to the decidua in the young placenta. His conclusion was that no sharp line could be drawn histologically between the long ago observed but rare malignant hydatidiform moles, and the new deciduomata. In both diseases the active element was the chorionic epithelium which had taken on an excessive and aberrant growth after the manner of the epithelial structures in carcinoma. Unfortunately, also, he was likewise forced to consider it impossible to distinguish sharply between the proliferation in a simple mole and that in a malignant one; a conclusion which still holds good. It is interesting to note that although he accepted the different origin of the two layers, he traced all the intermediate cell forms, and noted that this agreed with the older observations of Kastchenko who had believed in their common origin from fœtal epiblast.

According to the view of Marchand, then, the so-called deciduoma malignum or, as he called it in his monograph of 1898, chorionepithelioma, may be regarded as a member of a series of diseased conditions of the chorionic epithelium which shows many varieties, and a progression in degree of malignancy comparable with the progression

from simple adenoma to malignant adenoma or papilloma and carcinoma.

Like other malignant tumours, it has its physiological prototype, the characters of which it reproduces in an aberrant and excessive manner. The young chorionic epithelium, or to use the name which is now commonly applied to it, the trophoblast is an extremely peculiar and active tissue. Its structure is as characteristic as that of any other tissue of the human body; there is none with which it can be confused by anyone of reasonable histological skill. Physiologically also, it is quite characteristic, discharging, as it does, the functions in the first place of establishing a connection between the mother and the embryo, and, secondly, of maintaining it up to the time of birth.

In respect of the former, it shows indeed a striking resemblance to a malignant tumour. As Hubert Peters observed in comparing the trophoblast of the earliest known human ovum with the tumour, "The young trophoblast has a striking power of growth and in respect to its physiological relations in the early stages of the embedding of the ovum (destructive effects on the enclosing zone), does indeed manifest a destroying (malignant) action on maternal tissue." The villi of ova of slightly later date also show a very luxuriant growth of epithelium which is quite normal (Fig. 4) and even in the placenta of the third or fourth month villi may be found which show considerable masses of epithelium (Fig. 3).

The actual diseased conditions related to tumour may be classified as follows:—

(1) The simple hydatidiform mole, which may be a dangerous disease, even apart from any actual malignancy.

(2) Malignant hydatidiform moles, which differ from the preceding but little in their structure—a little more overgrowth of the epithelium, a little more infiltration of the decidua, the invasion of vessels and the establishment of metastatic growths, which may also contain villi, in the vaginal vessels and the lungs. In the combination of epithelium which is the essential malignant structure with a stroma which may show growth but no malignancy, this may be compared with malignant papillomata.

(3) The pure chorion-epithelioma in which no trace of fœtal mesoblastic tissue is to be found.

(4) Connecting these two, tumours composed almost entirely of epithelial tissue in which a few villi, either normal or more or less hydatidiform, are seen.

The tumours of the last class are the crucial ones in which the whole of the tumour tissue in all its varied cell forms can be traced directly to its source.

The relationship between the normal placenta, the moles and the

tumours was worked out in a masterly manner by Marchand, but a case of the last class to actually demonstrate his conclusions was yet wanting. A very interesting link was supplied by the consideration of the case of Meyer published in 1888, in which, sometime after the removal of a large hydatidiform mole in a woman aged 55 years, violent hæmorrhage and rigors set in, leading in a few months to a fatal issue. The uterus was considerably enlarged and shewed an irregular ulcerated internal surface. This was regarded as a tumour, and Meyer himself accurately indicated the chorionic epithelium as the essential element of the growth. Klebs, in his text-book of pathology, referred to the case as a beautiful example of "parasitism"—fœtal tissues invading and destroying the maternal—he called it a papillary epithelioma of the body of the uterus. Certain structures in it he regarded as chorionic villi to which the epithelial tumour belonged. Marchand referred to it as a link between the malignant moles and the chorionepitheliomata although he doubted if the structures described by Klebs as chorionic villi were really of that nature; he thought they were only masses of fibrin amid the epithelial cell masses.

In 1896, the gap was filled by the publications of Apfelstedt and Aschoff and of Julius Neumann. In their papers several cases of characteristic deciduoma malignum were described, in which villi were present and in which the origin of the tumour tissues from them was readily traceable. Other monographs followed in which the same connection was demonstrated. There is no clearer example of the tracing of a tumour to its physiological prototpye than chorionepithelioma. Such evidence there is no getting past.

Aschoff's paper also contained an admirable study of the normal placenta in which he came to the conclusion that the view then most generally held in Germany and which Marchand had accepted, that the syncytium of the chorionic villi was a derivative of uterine epithelium, while the Langhans' layer represented the fœtal epiblast was erroneous. His conclusion was that both layers were fœtal epiblastic in nature and were capable of being transformed one into the other. Marchand also, from further studies of the normal placenta, in his second paper (1898) inclined more towards this conclusion. He has now fully accepted it. About this date, too, the preliminary communications of Peters and Siegenbeek van Heukelom on extremely young human ova appeared. Both of them regarded the chorionic epithelium as purely fœtal epiblast, a conclusion which is adhered to in their complete publications. At any rate, Marchand was then clear that whatever might be the nature of

the two layers, the origin of the tumour from both of them was no longer open to question.

The effect of Marchand's work may be characterized as revolutionary. Nearly all authors who have published cases since 1895 have accepted his views, and many of the old ones have been re-described in the same sense. Gottschalk re-examined the cases of Tannen and Hartman and Toupet, and reported them as tumours of the chorionic epithelium in the sense of Marchand, abandoning his former view of sarcoma of the chorion. Schmorl, who had prepared the microscopic specimens of Sänger's original tumour, re-examined them and also declared in favour of the Marchand view. Sänger adhered to his old opinion. Subsequently he admitted that many of those cases might be epithelial tumours, and Austerlitz, in reporting a case from Sänger's clinic in 1902, gives what may rest as his final opinion. "Sänger accepts in essence the explanation given by Marchand, but with the reservation that the possibility of the formation of sarcoma cells out of decidua cells in respect to his first case, which does not correspond in all points with those of Marchand cannot be excluded." I have examined Schmorl's preparations and I am of the opinion that the original deciduoma malignum was a typical chorionepithelioma, many of the cells of which presented the resemblance to decidua cells, which is seen in all those tumours.

The opinion that a real sarcoma composed of decidua cells may occur is also held by Chiari. In conversation, Professor Chiari referred me to the case of Bacon reported from his laboratory originally as deciduoma malignum. In the year after the publication of Marchand's papers, this was examined and reported again (by E. Frankel) as a typical tumour of the chorionic epithelium. This, Chiari said, might be taken to represent the acceptance by his school of the Marchand view. Although he has not published any other paper on the subject, he had frequently expressed that opinion in meetings of societies, for example, in the discussion on Schlagenhaufer's communication at Carlsbad last summer, but he would make the reservation that a true deciduoma malignum may occur.

Dr. Whittridge Williams,* in a letter to me, states:—

> In view of the changes in embryology which have occurred since I wrote my article I have found it necessary to change my views upon the subject, and at present I believe that the syncytium as well as the isolated cells represent chorionic epithelium, and are derived primarily from the fœtal ectoderm. Accordingly, I share the views of the German

*Williams' *Obstetrics*, recently published, contains an excellent short account of the whole subject.

investigators who designate the growth as chorio-epithelioma, and only use the term deciduoma malignum from the clinical point of view.

This is practically the universal attitude of German pathologists. A few like Kossmann and Pfannenstiel, while agreeing that the tumour arises from the chorionic epithelium, have not yet accepted the above view as to the nature of that structure. The views of Marchand are also accepted by the Italian, French, Russian, Swedish, and American observers whose names will be found in the table of cases.

On the other hand, in 1896, the members of the Obstetrical Society of London, in a discussion on cases reported by Herbert Spencer, Malcolm, and Rutherford Morison, were for the most part opposed to the idea that there was anything special about these growths, and the Pathological Committee to which the specimens were handed over for full examination decided unanimously that the tumours shown to them were sarcomata; further that there was nothing in their histological characteristics to justify the supposition that they were of decidual origin, and that the term deciduoma malignum was therefore an inappropriate one.

In the discussion, the opinion of Marchand was quoted and the case of Apfelstedt and Aschoff was cited. In the report of the Committee, they are not directly referred to, but they seem to have had considerable influence in moulding that report to the extremely guarded form which it took.

In 1898, Dr. J. K. Kelly and the author reported the first case which was observed in Scotland. In sections of the secondary tumour in the lung we had the fortune to find masses of the young tumour tissue growing amid uncoagulated blood, and therefore presenting appearances unmodified by contact with the maternal tissues or by degeneration. Comparing this with our preparations of the placenta, we had no difficulty in recognizing the identity of the tumour tissues with the expansions of the chorionic epithelium which are seen particularly about the tips of the villi where they are attached to the decidua—the so-called "haftzotten," and we therefore accepted the view of Marchand. This lead has been followed by all who have reported cases in Scotland. The actual origin of the tumour from the villi has since been demonstrated in this country by Haultain and recently by Prowse.

The discussion in the Obstetrical Society of London was held at an unfortunate time when there was still great confusion regarding deciduoma. I think it was a pity, considering the amount of influence which their decision has had and the great clearing up of

difficulties which occurred within the two years succeeding their discussion, that they did not accept the advice tendered them by Marchand in 1898, and have a thorough reconsideration of the subject long ago. Certainly there was a discussion in London on Haultain's case. No preparations could demonstrate more conclusively than his the origin of the tumour, and the cases since then even in London have usually been reported as chorionepitheliomata.

On the Continent, practically the only opposition to the opinion of Marchand comes from the school of Veit. The essence of the tumour Veit holds to be sarcoma of the maternal tissues associated with pregnancy. He admits the presence of fœtal structures, but he regards them as adventitious. The course of events under his theory presupposes a sarcoma in the body of a uterus, which afterwards becomes the seat of a pregnancy. The case which he published was clinically a typical example of deciduoma malignum. The tumour presented quite characteristic appearances and contained a number of villi; large cells, many of them multinucleated, lined the adjacent blood vessels, and also appeared among the uterine tissues, including the muscle. These cells he regarded as sarcoma cells of maternal origin constituting the real tumour tissue. Evidence that they were invaders he could not find. The occurrence of pregnancy in a uterus already the subject of a sarcoma of the body he admits has not been demonstrated. This account of the sequence of events, although it has now been in evidence many years, remains purely hypothetical. Winkler, who has revived the old error of treating the syncytium as a derivative of uterine muscle, need not be considered. His more gross inaccuracies have been exposed.

In 1901, Veit published a paper on deportation of chorionic villi. That the metastasis of tumours has a prototype in the escape (deportation or Verschleppung) of portions of villi, or fragments of chorionic epithelium into the maternal vessels, was made known by the work of Schmorl on puerperal eclampsia some years ago. It has been confirmed by various observers—Lubarsch, Aschoff, Veit, and, still more recently, Poten—and I have also been able to observe it for myself in two specimens of the uterus with the placenta in situ. Williams has also observed it. Formerly it was supposed to occur only in diseased conditions, but it has now been observed under such circumstances as to favour the belief that it occurs in the majority of normal pregnancies. Usually the escaped materials undergo dissolution in the maternal blood, and give rise to no

symptoms, but under conditions about which little is known, they give rise to those abnormal cases of chorionepithelioma in which the primary tumour is situated outside the ordinary seat of implantation of the ovum. The fact of deportation, Veit demonstrated in a case of extrauterine pregnancy. That the deported villi may attach themselves to the interior of the maternal blood vessels just as they attach themselves to the decidua in their normal seat Veit allows,* but only under abnormal conditions of the maternal organism. He holds that disease of the mother cannot arise from the fœtus. Where the fœtus or placenta is diseased, the cause is always primarily in the mother.

From study of the Siegenbeek van Heukelom ovum he has satisfied himself that the theory of imbedding of the human ovum by removal of the uterine epithelium and attachment by means of fœtal epiblast to maternal connective tissue (Peters and van Heukelom) is probably correct in the main, but he will not admit that destruction of the maternal tissues or infiltration of maternal tissues by fœtal, after the manner of a malignant growth, has been demonstrated. The large supposed infiltrating cells in the decidua enclosing a normal ovum and in the walls of the blood vessels wherever deported villi are attached (which are generally accepted as derivatives of the chorionic epithelium) he regards as formed in situ from maternal elements—practically as decidua cells.

Thus the difference between the views of Veit and Marchand turns on the interpretation of the large infiltrating cells which Sänger originally regarded as the decidua cells composing the tumour. I shall return to this later.† In discussion with Professor Veit, I gathered that he is not quite so strongly of the opinion that those cells are not of fœtal origin, but even if he were to allow that point and abandon his view that the sarcoma is the primary element in the disease, he would still hold that some disease of the mother preceded the disease of the ovum.

The actual cause of these tumours is unknown. What the conditions of origin of the tumours might be, Marchand discussed in his publication. While admitting that there is much to be said in favour of the state of the maternal tissues being the cause, he considers the primarily fœtal origin to be the more probable. Either

*An interesting speculation on the influence of such deported villi I have encountered in the papers of Veit and Kollmann. This material, which becomes dissolved in the maternal blood, represents the male "germ plasm" as well as the female. It is suggested therefore, that it may be the material basis of telegony!

†Histological details, p. 45 et seq.

observer might be right without in any way disproving that the actual tissues which behave as tumour are fœtal.

Whatever may be thought as to the source of chorionepithelioma, the connection with pregnancy is beyond question. This is so clear from the clinical facts alone that it is hardly worth discussion. Even excluding the malignant moles, there are many cases in which the disease was continuous with the pregnancy. Cases there are in which the clinical history shows an interval greater than one year between the pregnancy and the first symptoms of disease, and in several the preceding pregnancy was not clearly demonstrable; but one is quite justified in treating these as exceptional. Tumours which do not show that feature should be accepted as chorionepitheliomata only on the clearest histological evidence being produced.

I regard the controversy, then, as having been brought to an issue by Marchand in his paper of 1898, and I think that his theory that deciduoma malignum and destructive (malignant) hydatidiform mole are diseases of the chorionic epithelium might at that date have taken a place among the proved facts of pathology. What remained still open for discussion was the expiscation of all aberrant forms of the tumour, the question of diagnosis and treatment, and the problem of the nature of the chorionic epithelium. The last we shall now proceed to consider.

The Physiological Prototype of Chorionepithelioma.

Our knowledge of the structure of the placenta is much more favourable to a consistent explanation of the peculiarities of the tumour at the present time than it was in 1896. The fœtal epiblastic nature of the whole chorionic epithelium seems to be proved. The magnificent monograph of Hubert Peters on the earliest stage of human placentation yet discovered seems to leave little room for doubt; notwithstanding that the veteran Langhans still holds the uterine epithelial origin of the syncytium to be discussable for the human subject, and Selenka in the last part of his work on the apes maintains that in them "the uterine epithelium plays an important rôle" in the formation of the placenta. In my opinion, the conclusion of Peters must be held valid unless material yet more favourable than his unique specimen should be found and should demonstrate the contrary.

All the literature of human, and, in less detail, comparative placentation up to 1899 is reviewed by Peters; an excellent summary of the subject, containing evidence of much original research, and

giving a very full account of Peters' work has recently been given by Clarence Webster in his "Human Placentation." The position of the comparative anatomy of the placenta is indicated in some of the more recent papers of Hubrecht in German, and is summarized in English by Jenkinson.

The description of the placenta is best approached by considering its structure in the second month. Abortions of six to eight weeks are fairly easily obtainable. After the fourth month retrogressive changes have advanced so far that for the most part only the one layer of the epithelium—the syncytium—remains. The decidua ever since William Hunter recognised that it was the uterine mucous membrane modified to subserve the needs of pregnancy, and first described its gross relations to the ovum, has been regarded as a maternal tissue. The decidua vera presents no difficulty, and contains no elements about which doubt can arise; the similar tissues in the serotina and reflexa are judged by comparison with it. The problems are connected with the so-called epithelial wandering cells of the decidua serotina and the epithelium of the chorionic villi. Taking the villus in the early stage, say about the sixth week of gestation, the mesoblastic stroma containing the blood vessels is found to be enclosed in a double layer of epithelium. This fact was recognized by Goodsir and S. von der Kolk (according to Virchow), but the classical description we owe to Langhans.

The epithelium consists of—

(1) An inner single layer of cubical cells having clear protoplasm and round or oval vesicular nuclei of relatively large size, moderately rich in chromatin and showing a well-marked intra-nuclear network and nucleolus; multiplication is by indirect division, and karyokinetic figures can usually be found without much trouble. The protoplasm contains glycogen. This is known as Langhans' layer, and the cells as the individual cells. They rest on the connective tissue core, the line of junction often being a well-marked basement membrane.

(2) Enclosing that and separating it from the maternal blood in the intervillous space is the syncytium, a layer of protoplasm in which no definite cell boundaries are recognisable. The protoplasm has an opaque appearance, and takes the usual contrast stains somewhat deeply. In specimens fixed with osmic acid it is usually found to be richly loaded with finely-divided fat. The nuclei are generally smaller than those of the Langhans' layer, oval or more elongated in shape, solid, and staining more deeply. The appearances, and especially the distinctness of the two layers, vary considerably according to the state of preservation and the character of the fixative agent used. In material which is not very fresh the distinction may be difficult to make out. The syncytium frequently spreads out into buds, which may even be detached from the main layer and lie apart as multi-nucleated giant cells free in the maternal blood, or it may be merely a thin layer resembling endothelium. The free edge of the

syncytium shows more or less distinctly a fringe of protoplasmic processes which have been described as cilia, but they are not of this nature, being non-motile. Doubtless they have to do with the absorptive and secretory functions of the epithelium. A better comparison of them would be to the striated border of the intestinal epithelium or the fine processes in the prickle cells of the epidermis.

Here and there the Langhans' layer spreads out into masses of considerable size. These occur in the intervillous space (forming cell knots), but are best developed at the attachments of villi to the decidua—the haftzotten or villi of attachment. At these points they form a layer several cells deep between the tip of the connective tissue core and the tissue to which it is attached. The cells composing these masses commonly retain their clear protoplasm, but both nucleus and cell body tend to be considerably increased in size. The syncytium instead of enclosing these cell masses divides on either side, and is applied to the surface of the decidua lying between the attachments of villi. At this stage there is commonly no mingling of the Langhans' layer cells with the decidua, the two being separated from one another by what is usually called the canalised fibrin layer (fibrin layer of Nitabuch), a dense stratum of necrosed tissue mixed with fibrin.

The cell knots often contain more or less fibrin or degenerated material, and the cells then tend to be enlarged and altered in character. Thus they may form masses of somewhat large cells with very large nuclei more or less embedded in fibrin, which present a superficial resemblance to the decidua cells. They were formerly regarded as processes of decidua; now, however, their origin has been traced from the chorionic epithelium. Apparently for the most part they are derivatives of the Langhans' layer, the modification being of the nature of hypertrophy with more or less of degeneration, the exact limits of the two processes being very difficult to determine.

Masses of what are plainly syncytium may also be seen in those cell knots, and there are cells also mono-nucleated or with two or three nuclei, but with the opaque protoplasm characteristic of the syncytium. In the decidua and in the fibrin layer lining it, similar cells may be observed. There are also large isolated cells with protoplasm similar to the syncytium and multiple nuclei to be found in varying number in the decidua, and even in among the uterine muscle cells. These are generally taken to be infiltrating detached buds of the syncytium and are referred to as " syncytial wandering cells."

In the cell knots and masses at the tips of villi all forms intermediate between the typical individual cells and the syncytium have been described. In my preparations, however, the two layers are in general sharply defined from one another. This question of the transformation of the one layer into the other will be taken up under the histology of the tumours. The infiltrating giant cells and large individual cells are found in the decidua serotina and reflexa, but not in the decidua vera.

The idea that the placenta was an organ of mixed fœtal and maternal origin may be traced to William Hunter. According to him the villous chorion was everywhere interpenetrated right up to the membrana chorii by processes of decidua. In the joint organ there were two circulations which were quite distinct, the interchanges between mother and fœtus being by " transudation "; the

fœtal blood flowed through the vessels of the villi, while the maternal circulated in the "intermediate spaces" (intervillous spaces) which he compared to the cells of the corpus cavernosum penis. He regarded the placental cells as an extension of the maternal circulation.

The influence of these views is seen in many of the theories which have been held as to the constitution of the organ. By Reid, for example, it was supposed that the lining membrane of the maternal vessels was everywhere applied to the surface of the fœtal tissues, and the intervillous space was therefore actually dilated maternal vessels. The later representative of this was the view which interpreted the syncytium as a derivative of maternal endothelium (Winckler, Waldeyer, and Pfannenstiel). Langhans, in his classical description, regarded the inner layer as fœtal mesoblast, while the syncytium he regarded as fœtal epiblast; but he abandoned this view, and, along with many others, came to regard the syncytium as a proliferation of the uterine epithelium (the old view of Goodsir and Turner), while the Langhans' layer cells represented the fœtal epiblast. The revival of this particular opinion was largely due to the comparative anatomical studies of Selenka, Strahl, Gunser, and Kossman; and Merttens and Keibel appeared to have rendered it fairly probable for the human subject also. By 1895, the view that both layers were of fœtal epiblastic and therefore of common origin, which had been held by Minot and Kastchenko, was generally discredited in Germany.

On the other hand, others had observed (Hensen and van Beneden) that in the embedding of the ovum in rodents and bats, the uterine epithelium was destroyed and the ovum appeared to attach itself to the deeper maternal tissues. In 1889, appeared Hubrecht's monograph on the placentation of the hedgehog and about the same time Duval's on the placenta of the rodents (rabbit and guinea-pig) in which the disappearance of the uterine epithelium and the attachment of the ovum to maternal connective tissue by a proliferation of fœtal epiblast was described from most complete material worked up by histological technique of a very high order.

Huxley, in his paper on the application of the Law of Evolution to the arrangement of the mammalia had indicated the insectivora as a very central and primitive type. In the hedgehog, in particular, "we possess the key to every peculiarity which we meet with in the primates, carnivora and ungulata." Fairfield Osborne and other American paleontologists have since confirmed this position. On these grounds it was that Hubrecht chose the hedgehog for placental

research. To the naked eye its placenta also strongly resembled the human.

Hubrecht was able to demonstrate the manner of the embedding of the ovum of the hedgehog in the uterus, tracing it from the stage while it was yet free in the cavity through all stages of development up to the mature placenta. At an early stage of segmentation it comes to rest in a hollow or furrow in the uterine mucous membrane. Around it the mucous membrane swells up, forming a deep cleft in which the ovum lies. Then the epithelium in the immediate vicinity of the ovum degenerates and disappears. A similar fate overtakes the adjacent subepithelial structures. Maternal blood-vessels in this way are opened and a certain amount of hæmorrhage occurs around the ovum. The extravasated blood coagulates and the ovum is cut off from the uterine cavity by a plug of blood-clot which glues together the lips of what is now termed the decidual swelling. As segmentation advances the ovum is differentiated into two classes of cells, an outer set and an inner set. The inner, the hypoblast, remains comparatively small in amount; the outer, the epiblast, proliferates rapidly into a thick layer of cells, which at one part becomes still thicker, and projects inwards against the hypoblast. The greater part of the epiblast—in fact, all except that knob of cells lying towards the centre of the ovum—takes no part whatever in the formation of the embryonic shield, but becomes specialized as an organ for the nutrition of the ovum. This thick layer of primitive epiblastic cells, Hubrecht named on account of its nutritive function, the trophoblast, or otherwise trophic epiblast. In the early stages of development, the trophoblastic portion grows much more rapidly than the embryonic portion of the ovum, and thus the condition is attained of a relatively large nutritive organ enclosing a very small embryonal rudiment. Stated without details, the development of the placenta may be described as follows:—

Around the ovum destruction of the maternal tissues occurs to a considerable extent, the degenerated remains probably being used up by the trophoblast for its nourishment. Then a reaction in the maternal tissues outside the zone of destruction sets in and they begin to proliferate, forming what is called in the human subject, the decidua. An equilibrium becomes established between the trophoblast and the proliferating uterine tissues, union of fœtal and maternal tissues then takes place and where maternal blood-vessels have been opened the trophoblast becomes hollowed out into a sponge work of cavities containing maternal blood. This does not coagulate. On the contrary, the cavities take the place of vessels, become as it

were a part of the maternal circulation, and a primitive placenta is complete. There has been no extension of the maternal endothelium into these cavities to form a lining to them. Like the maternal epithelium, the endothelium in contact with the trophoblast simply disappears and its place is taken by fœtal cells. Later, with the growth of the embryonic rudiment and its differentiation into the three primitive layers, the fœtal mesoblast, bearing blood-vessels, enters into combination with the trophoblast and villi are formed consisting of cores of fœtal mesoblast covered with trophoblast which thus becomes the epithelium of the villi, and the cavities in it the intervillous spaces.

Here then is a proper placenta containing a circulation of maternal blood and a circulation of fœtal blood, the tissues of which are entirely fœtal. In the early stages, Hubrecht recognized a considerable proliferation of the maternal endothelium, and along the edge of attachment of fœtal to maternal tissues it was far from easy in the later stages to draw a sharp line between them. Recently one of his pupils, van Resink, has re-examined the hedgehog preparations and material, and his results in the main confirm the earlier ones. Where they differ it is in the direction of still further limiting the share of the maternal tissues in the formation of the placenta. The proliferating maternal tissues, especially the endothelium of the vessels, form a layer which Hubrecht called the trophospongia. The greater part of this and the layer of large multinucleated cells called deciduofracts, he now regards as part of the trophoblast. The trophospongia, as at present defined, is in the fully developed organ, a very thin layer. All the organ which performs the metabolic interchanges between mother and fœtus Hubrecht now regards as of fœtal origin.

The work of Duval led to results practically identical. The organ of attachment he found to be a proliferation of fœtal epiblast which he named ectoplacenta; a term which may be treated as synonymous with trophoblast. Later, Duval came to similar conclusions for the cheiroptera, and Van Beneden who had favoured other views in his earlier work on the same order stated in a letter to Duval his conversion to those of the latter. Nolf also brought confirmatory evidence.

Hubrecht forecast that the attachment of the human ovum to the uterus and the formation of the decidua reflexa would be found to resemble what occurred in the hedgehog; his hypothesis may be taken as the modern representative of the old idea that the decidua reflexa is formed by the rising up all round the ovum of a fold of

uterine mucous membrane, the edges of which eventually meet and unite over it.

A different mode of formation of the decidua reflexa was suggested by von Spee. Following up the work of Hensen on the guinea-pig, von Spee was able to confirm his observations that the ovum in that rodent breaks through the uterine epithelium between the mouths of the glands and burrows into and embeds itself in the connective tissue. Von Spee pointed out that this form of embedding would account for the fact that in his very early human ovum (of 11mm. longest diameter) no glands opened into the cavity of the decidua reflexa as they would on Hubrecht's hypothesis, and there was no lining of uterine epithelium to that cavity. His observations at that time (1891) were still incomplete and his full account of them has only recently appeared; even this covers only the embedding and not the formation of the placenta. But it covers the most important stages. The hole in the epithelium is blocked by the last part of the ovum remaining in contact with the edges; here at first there is no widespread destruction of the epithelium. Round the rest of the periphery of the ovum, the maternal cells swell up and gradually lose their distinct outlines and flow together into a symplasma or syncytium of degenerative nature. This was erroneously described by Selenka as developing into a part of the placental epithelium. Instead, it gets broken down into a fluid (histolysis), and by its destruction a space (implantationshof) is formed for the ovum to grow in. Outside the zone of degeneration, there is a proliferation of the maternal tissues into a " sort of granulation tissue that about 10 to 16 hours after the commencement of implantation perhaps hinders or at least limits the destruction of the uterine tissues."

Professor Graf von Spee showed me some of his later stages along with those already published. I think there can be no doubt that in the guinea-pig, as in the hedgehog, the ovum, " like a sort of parasite," attacks and destroys the maternal epithelium and underlying tissues until it forms a cavity in which to rest. Reaction of the maternal tissue follows, as round a foreign body, and the result is embedding of the ovum in maternal connective tissue by means of a proliferation of the fœtal epiblast.

Study of the convenient rabbit here as elsewhere in embryology has had results by no means happy. The uterine epithelium in the pregnant rabbit exhibits extensive formation of syncytium. This has been, and still is, regarded by many observers as the syncytium of the placenta, and they have applied the results without reservation

to the syncytium of the human placenta. The other interpretation appears to me more probable, according to which this is a mere temporary structure which disappears when the trophoblast comes into contact with it. I have preparations which show this disappearance, but they are too few to allow me to form an independent judgment on the whole question. As to mice and rats, opinions likewise differ. Jenkinson holds that the entire trophoblast is fœtal epiblast. The lower orders of mammals in which proliferated uterine epithelium is persistent differ so radically from the human subject in placentation that they need not be considered.

The hypothesis of Hubrecht, while in details different from that of von Spee, is in full agreement with it so far as the main principles are concerned. There is no essential opposition between the two. In 1893, Berry Hart and Gulland, in an admirable study of human placentation in material from the fourth week onwards, recognised that there was no proliferation of maternal tissues forming the chorionic epithelium, but, on the contrary, there was evident destruction of uterine epithelium and endothelium. The chorionic epithelium was described very much as I have described it; both layers they regarded as of common origin and fœtal epiblastic nature. They adopted Hubrecht's terminology in so far as to apply the name trophoblast to the cellular expansions at the tips of the villi and recognised its destroying action on the decidua. As a working theory, they put forward "the hypothesis that the human ovum could only graft itself on connective tissue, a view which might be added to Hubrecht's speculation." It was probable that it embedded itself by destroying a portion of the superficial epithelium and boring into the decidua (as Spee had already suggested). On the other hand, they thought that the removal of the epithelium was due to menstruation which prepared a suitable place on which the ovum might ingraft itself. The human ovum then was an "embedded one," not attached to the serotinal epithelial surface and with the epithelial vault of the serotina arching over it to form the so-called reflexa, but one actually growing in the serotina. The fœtal epiblastic nature of the chorionic epithelium was also maintained by Clarence Webster in his work on extrauterine pregnancy.

Placentation differs greatly in different orders and even in different species in the same order. Each ovum seems to be a law unto itself. Therefore, great caution must be exercised in applying the results of comparative research to the attachment of the human ovum.

Nevertheless, it appears highly probable that the problems of the

formation of the decidua reflexa and the nature of the placenta have at last been solved. The demonstration that the human ovum is an embedded one has come only with the discoveries of Hubert Peters. The same observer and Siegenbeek Van Heukelom have apparently proved the fœtal epiblastic nature of the human trophoblast and its later form the epithelium of the chorion.

The Peters' ovum is the only one yet discovered in which the decidua reflexa is not complete. According to the evidence it affords, the embedding resembles that of the guinea-pig ovum more than that of the hedgehog. Instead of being enclosed by swelling up of the mucous membrane around it, which would be equivalent to the old circumvallation theory of the formation of the decidua reflexa, the ovum bores its way into the mucous membrane, destroying the epithelium and underlying maternal tissues until it has reached a sufficient depth. The hole by which it entered is closed over it by a blood-clot. The Peters' ovum shows this stage quite clearly.

The pregnancy was probably not more than five or six days duration. It was obtained from the body of a woman, who on the non-appearance of menstruation along with the occurrence of subjective symptoms suggesting pregnancy (vomiting), swallowed caustic potash solution, and died in about three hours. Three hours later the uterus had been opened and the ovum discovered by prosector Kretz, who presented it to Professor Peters. The area of decidua containing the ovum was at once removed and placed in Müller's fluid which at first was changed every hour. After fixation it was embedded in paraffin and converted into an unbroken series of sections about 10 microns in thickness.

The Peters' ovum has been much criticised. It has been said that as it was taken from a dead body, it could not be fresh enough to be reliable; that it is badly fixed; that it is pathological; and that even it is not early enough to prove the nature of the chorionic epithelium. By the kindness of Professor Peters, I was able to study the preparations, and my impression is that it is a thoroughly reliable specimen. More favourable circumstances one could hardly have. The fixation is exceedingly good. It has the faults of Müller's fluid fixation to a slight degree—the cellular details are less clear than is the case by certain other methods of fixation. Otherwise there is no fault that can be found with it. It was not possible to study the distribution of glycogen or fat. It has recently been re-stained with hæmalum and eosin, and the structure of the trophoblast is now plainer than when the original description was written, but no changes require to be made. Probably the spaces of the trophoblast are somewhat overfilled with blood, but certainly to a much less degree than is the case in the other early ova which I

have seen, and not to an extent which in any way disturbs the relation of parts. Apparently there has been a considerable degree of congestion of the uterine mucous membrane.

Further, no one can say that it is pathological, for there is no other so young with which to compare it. Considering it as the youngest member of the series consisting of von Spee's 3 ova (one as yet unpublished) the Van Heukelom ovum, and the two youngest Leopold ova (all of which I have examined) one can have no hesitation in accepting the opinion of von Spee that it is normal, as fully warranted. From the point of view of histology as distinguished from that of embryology, Marchand and von Spee agree in regarding it as irreproachable. For those to whom the original is inaccessible, the account of this ovum by Webster can be highly recommended, but there is no work which can fill the place of the original monograph.

The ovum, which measured 1·6 by 0·8 by 0·9 mm., is completely embedded in somewhat œdematous tissue. There was no projection of the decidua over it, and it was discovered by Dr. Kretz only by the detection of a paler area in the somewhat thickened and congested mucous membrane covering the posterior wall of the uterus. The greater part of the uterine mucous membrane shows only a condition of swelling, true decidua formation having commenced only in the immediate neighbourhood of the ovum. The ovum itself consists of a thick sphere of trophoblast, which is irregularly hollowed out by spaces containing maternal blood. Within that the embryonal rudiment, consisting of a very small epiblastic shield with the amnion already closed over it, and the rudiment of a yolksack and a very small amount of mesoblast between them is slung in a network of delicate connective tissue—the extra-embryonic mesoblast or mesoblast of the chorion—which connects it with the trophoblast. There are no fœtal blood-vessels and no signs of an allantois. The outermost layers of the chorionic mesoblast are somewhat denser than that filling the general cavity of the trophoblast. The surface shows a few slight projections in it, corresponding to depressions of the trophoblast, but actual formation of villi had not yet taken place. Between the mesoblast and trophoblast in places is a slight cleft which is artificial. The innermost layer of the trophoblast consists of small cubical cells exactly corresponding to those of the later Langhans' layer. External to this and obviously continuous with it are considerable masses of cells which are somewhat larger and show much larger nuclei; and between these and the blood in the spaces of the trophoblast is a complete layer of syncytium which in some parts is in considerable masses, in others is so thin as to look like an endothelium lining the blood spaces. Both by the relatively large size of its nuclei and the character of its protoplasm it differs entirely from real endothelium. The appearance is one I am familiar with in the tumour and in the normal placenta. Its interpretation presents no real difficulty.

In the large cell masses of the trophoblast Peters can trace all the intermediate forms between the individual cells and the syncytium. The primitive type of cell is the clear cubical mono-nucleated cell of the inner layer. Where the trophoblast is united with the maternal tissues the

individual cells appear to be in contact with the connective tissue, and there is a certain degree of mingling of fœtal elements with maternal elements. Outside the zone, which is clearly trophoblastic, are seen large cells, sometimes multi-nucleate, which Peters takes to be wandering elements of the syncytium. In the maternal tissues, although there is a slight modification of some of the cells in the direction of decidua cells, and apparently new formation of blood-vessels, there is no such proliferation as even to suggest that the trophoblast had developed out of the maternal tissues. On the contrary, there is clear evidence of destruction of the maternal tissues where they are actually in contact with the trophoblast. In special the uterine epithelium, both of the surface and of the glands, in the immediate neighbourhood of the ovum gives evidence of degeneration, and the destruction of the maternal endothelium is also clearly demonstrated.

The work of Van Heukelom on a somewhat older ovum which was obtained in conditions almost equally favourable for the study of the relationships between the fœtal and maternal tissues also led to the conclusion that the whole trophoblast is of fœtal epiblastic origin. The broad lines of distinction between fœtal and maternal tissue are quite clear. With regard to cells here and there, there is admittedly a difficulty which is experienced in all placental research, viz., that the union between the maternal and fœtal is so intimate, and the variety of cell forms appearing in the border zone is so great that there are some cells about whose origin one would not commit one's self to a decided opinion. This is the case even where, as for example in the work of Hubrecht on Erinaceus, Tarsius spectrum, and Tupaja javanica (insectivora), the material contains all stages from the free ovum in the uterine cavity up to the mature placenta; but this does not affect the main principles.

The only member of the primates which has been worked out with full material is the curious aberrant one, formerly classed with the lemurs—Tarsius spectrum. In this, Hubrecht finds the connection to be established by a process homologous with that in the hedgehog. The ovum in this case is not wholly embedded; the trophoblast developes over a limited area only. The completely fœtal nature of that structure is very clear in this animal.

The true monkeys and the apes would perhaps be as well left on one side just now. Turner and Waldeyer found a very close resemblance between the placenta of the monkeys and the human placenta. Selenka described the villi as covered by a double layer of epithelium exactly similar to that in the human placenta. The syncytium, he regarded as formed by proliferation of the uterine epithelium, while the individual cells represented the fœtal epiblast. This opinion was controverted by Hart and Gulland, who considered

the chorionic epithelium in the monkeys to be of the same nature as they had described for the human subject, and they considered that Selenka's illustrations did not prove his view. Kollman recently has expressed the same opinions. In the last part of Selenka's great work recently issued "as a fragment" under the editorship of Keibel, he still adheres to the opinion that in the formation of the ape's placenta, the uterine epithelium plays an important rôle. It is probably better, however, seeing that the work is but a fragment, to leave the placenta of the apes entirely out of account until we have the promised complete description of Selenka's material by his pupils Hubrecht, Strahl and Keibel.

In concluding this part of my paper, I have to acknowledge the great kindness of Professors Peters, Hubrecht, Marchand, von Spee, Veit and Dr. Leopold, in not only allowing me to see their preparations, but in giving valuable time to demonstrating them to me.

Addendum. Since the above was written three important papers have passed through my hands, viz., those of Sobotta on the "Development of the ovum of the mouse," of Hitschmann and Lindenthal on the human placenta, and of Andrews on "tubal pregnancy." All of these confirm and strengthen the position which has been maintained in the preceding pages.

Reports of the Cases.

Of the three new cases, two are quite typical examples of chorionepithelioma arising after abortion. The third must be classed as a doubtful case, being possibly only hydatidiform mole. The case formerly published along with Dr. Kelly forms a good supplement to the group. All the new cases were submitted to operation. That of Dr. Kelly shows the course of the disease in the very malignant type, undisturbed by operation. It is, therefore, recapitulated at some length.

Case of Kelly and Teacher.

Clinical History. February 2nd, 1897; Mrs. L., aged 27, 2-para, now in her third pregnancy, consulted her medical attendant on account of slight hæmoptysis. This was supposed to be due to incipient phthisis as the expiratory murmur at the apex of the right lung was prolonged. This slight hæmoptysis recurred from time to time. Probably it was not connected with the growth. On April 20th there was some vaginal discharge.

On June 18th labour came on, and a mole about the size of a Jaffa orange, which was not hydatidiform, was expelled. No tumour was then observed in the vagina. Hæmorrhages from the vagina continued to occur, and on August 7th a small tumour like a foreign body, about the size of a shilling, lying on the anterior wall, was detected. An attempt

to remove it caused such severe hæmorrhage that the vagina had to be plugged.

On August 10th "an ulcerating hæmatoma" was removed from the anterior vaginal wall. It was not examined microscopically. Bleeding having persisted, the patient was removed into the Royal Infirmary on the 20th of September. At this time there was an elongated finger-like mass in the anterior vaginal wall and a rounded nodule in the posterior wall, and the uterus itself was enlarged. On the 24th of September there was a severe uterine hæmorrhage, followed by collapse of the patient. On the 28th of September a slight cough commenced with streaks of blood in the sputum. On the 3rd of October recurrence of the uterine hæmorrhage; thereafter rapid increase in the size of the uterus and decline of strength; death on the 19th of October—four months after the abortion.

The body of the patient appeared well nourished, but was extremely blanched. The *post-mortem* examination showed that the lungs were the seat of numerous secondary nodules, but the other organs of the thorax and the abdominal organs presented no important abnormality. The uterus was about the size of the pregnant organ at the end of the fourth month. The enlargement affected particularly the posterior wall and fundus, which were rounded out by the tumour. This surface of the uterus was of a peculiar mottled red and pink colour owing to the large amount of blood in the tumour, which had almost reached the peritoneum. In the right Fallopian tube there was a small globular nodule of dull red colour enclosed in a thin capsule of tube wall. Several rounded tumour masses projected into the vagina. The lymphatic glands in the neighbourhood of the rectum are said to have been enlarged, but they were not kept for microscopic examination.

The uterus was opened by an incision right through the tumour. This filled the whole cavity. It rose from the fundus and posterior wall. In section it presented the appearance of blood-clot mixed with lighter coloured strands of tissue. In its outer part it, to some extent, resembled placental tissue. The uterine muscle had been almost completely destroyed in the seat of the tumour, but there was not any actual perforation.

The rectum and bladder were not involved. Dense swellings could be felt on either side of the vagina and cervix which, on dissection, were found to be secondary tumours, partly in the vesical, uterine and vaginal veins, partly in the lymphatic glands in the base of the broad ligament. Separate from these there were a number of nodules which looked like thrombosed varicose veins. They were in fact veins dilated by tumour invasion. Along either side of the vagina, extending about half-way to the ostium, were large masses of the same nature, in appearance exactly like thrombosed varicose veins. This is the usual description of these vaginal metastases.

The tumours in the base of the broad ligament were about the size of a walnut. They were quite detached from the side of the cervix uteri, separated from it by a thin layer of normal tissues through which the ureters were traced. The blood-vessels between these nodules and the uterus were not thrombosed. The microscopic examination demonstrated that the lymphatic glands were involved in the tumour, and at the time the authors were inclined to regard this as a proper lymphatic infection. The proof of this, however, is not absolute. Lymphatic gland tissue there is in the nodules, but the relations of the tumour tissues to it do not preclude the possibility that, even as emboli had fallen down into the

vaginal veins and given rise to secondary tumours there, so they may have rested in the iliac veins about the junctions of the vesical uterine and vaginal branches, where they attached themselves and grew outwards, thus invading the lymphatic glands.

Lymphatic infection is quite exceptional, having been recorded only in eight cases, all of these being very advanced. In case 2 of Marchand (Everke), the relationship of the tumour cells to the lymphoid tissue appears to prove that they were infected through the lymphatics. In two cases—Winkler and Menge—the bronchial lymphatic glands were involved. On the other hand, metastasis by way of the blood stream has been recorded in the majority of the fatal cases. For this tumour, as for sarcoma, it is the usual route.

Microscopic examination of the primary growth showed that, as usual, by far the greatest part of it was composed of blood-clot mixed with a certain amount of necrosed tumour tissue. The actual living tumour formed the floor of an extensive ulcer, as it were, between the blood-clot and the uterine muscle. Plugs of it burrowed in among the muscle fibres and along the cavities and walls of the veins. Thrombosis of the larger veins near it was common, but the thrombi were of quite recent formation—probably not long before the death of the patient. The mucous membrane was in a condition of ulceration and inflammation. Decidua cells were not observed.

The lungs were studded with round firm nodules of a dull red colour; those on the surface projecting somewhat. In section they were rounded, and well defined, and did not, as a rule, present much resemblance to either hæmorrhagic infarcts or pneumonic patches except in colour. They had a drier, older, and better defined appearance. They were composed principally of blood-clot with living tumour tissue recognisable only around the edges. The neighbouring alveoli contained red blood corpuscles, catarrhal cells, and some plugs of fibrin.

The diagnosis of the tumour as a derivative of the chorionic epithelium was made, as already mentioned, from one of these secondary nodules in which masses of very well preserved tumour were found growing in fluid blood. The resemblance of these to the masses of Langhans' layer and syncytium around the attachment of villi to the uterine tissues in the normal placenta was so exact that it was impossible to doubt their identity and little difficulty was experienced in determining that the other elements in the tumour were derived from these two structures. Actual villi were not present in either the primary or the secondary tumours.

The destructive action of the tumour tissues on the walls of the

blood vessels was very clearly recognised in dissecting the masses at the side of the vagina and cervix. The walls of the large veins there were quite rotten and microscopic examination demonstrated that this was due to their erosion by infiltrating processes of tumour cells.

Another point which may have an important practical bearing was the condition of many of the secondary nodules. The tumour in the fallopian tube and several of the small intravenous nodules were very dense, and, on being incised, shelled out of their capsules. Serial sections were prepared to investigate the reason of this and demonstrated that the entire tumour tissue in the nodule was in a state of necrosis. Various observers, from Gottschalk onwards, have commented on this apparent destruction of the tumour by the hæmorrhage which it has itself evoked, and some, *e.g.*, Haultain, have regarded it as a possible explanation of the fact that patients have recovered after removal of the primary tumour, although symptoms pointed strongly to the occurrence of metastasis in the lungs. This will be referred to further in discussing the question of prognosis and treatment.

New case, No. 1. Dr. John Edgar's. To Dr. John Edgar I have to express my indebtedness for the specimen, for the clinical notes of the case, and for many valuable suggestions.

History. Mrs. P., aged 32, married six years, no children. Her health previous to 1897 was good, menstruation was regular every four weeks. On the 29th of March, 1897, she aborted after two months' amenorrhœa. There had been no morning sickness and no breast symptoms. Dr. Burges removed the ovum with his fingers. The subsequent hæmorrhage was slight, and only lasted for a day or two. On September 6th, 1898, there was a second abortion like the first, but breast symptoms were present, and the ovum came away spontaneously. In November, 1898, the patient had an attack of appendicitis. In February, 1899, Dr. Burges inserted an intrauterine stem pessary on account of ante-flexion of the uterus. In March, 1900, Dr. Burges dilated the cervix uteri. This was done not because of dysmennorrhœa, but because of the patient's desire for pregnancy.

On September 20th, 1900, after two months' amenorrhœa with breast symptoms but no morning sickness, the patient sent for Dr. Burges on account of uterine hæmorrhage. It was slight, and lasted only a few hours. There was no pain. Thereafter there was a slight but almost constant bloody uterine discharge, dark in colour and odourless. In December this increased in quantity, and became red and mixed with clots. On the 18th of December a fleshy mass about the size of a hen's egg was extruded into the vagina, and was removed by Dr. Burges. He states that it did not look like an ovum. He regarded it as fleshy mole, but did not keep it nor get it examined microscopically. He is certain that it was not a vesicular mole.

The bleeding continued until the 1st of January. A few days later a

slight brown discharge reappeared. On the 7th of January intra-uterine application of Ac. carbolic; on the 23rd of January severe rigor with pyrexia lasting three hours. On the 7th of February Dr. Edgar removed with the curette several small pieces of tissue like placental remains. Microscopic examination gave no definite results. The discharge ceased.

In July it reappeared after a menstrual period, which had been delayed a week and continued off and on. On the 31st of August Dr. Burges was called in on account of the increase of the discharge. On the 3rd of September there was a second pyrexial attack, beginning with a rigor and lasting a few hours. On the 5th of September Dr. Edgar curetted a second time, and brought away pieces of tissue similar to the last. No definite result was obtained from microscopic examination of these pieces, but the clinical features of the case were so suggestive of deciduoma that on the 25th of September another portion was removed and sent to me. Characteristic masses of tissue were found in this. On the 5th of October, 1900, Dr. Edgar performed vaginal hysterectomy.

The operation was a difficult one owing to the narrowness of the vagina and the size of the uterus. Clamps were used instead of ligatures. They were removed in 48 hours. Dr. Burges states that the uterus was reduced in size by the curettage of 5th September, and then rapidly enlarged. The hæmorrhages recommenced on the 10th. Just after the operation the patient spat up a mass of tough, bloody mucus. Microscopically it showed recently shed blood and a considerable number of leucocytes and catarrhal cells. There were no elements suggestive of deciduoma malignum. Tubercle bacilli could not be detected. The tubes and ovaries were left. Dr. Edgar examined them. There was no sign of secondary growths in them nor in the veins of the vagina and broad ligaments. Patient was dismissed on the 20th of September, well.

Description of the Tumour. The uterus was pear-shaped and considerably enlarged, measuring in total length 14 cm., of which 8 cm. was body. The breadth between the tubes was 8 cm., the thickness back to front 6½ cm. The cervix was lengthened, measuring 5 cm. by 3 cm. by 2·2 cm. The enlargement of the body was directed towards the right cornu, and the uterus bulged more in front than behind. There was no sign of tumour externally. A few inflammatory adhesions over the posterior surface had to be torn before removal could be effected. On slitting open the uterus from the anterior surface the cavity was found to be considerably dilated; the tumour covered the fundus and extended down both the anterior and posterior walls for some distance to within about 2·5 cm. of the os internum. On either side there was a wedge-shaped area of mucous membrane, free of tumour, running up into the Fallopian tubes, which were quite clear. The tumour was a somewhat dense, fleshy mass of dull red colour with a few hæmorrhagic patches in it. Its surface for the most part did not appear to be ulcerated. In section the tumour seemed not to infiltrate the uterine muscles but to lie on it, projecting into the cavity of the organ. Towards the growing edge especially bands of the uterine muscle appeared drawn up into the tumour. (Figs. 1 and 2.) It looked as if composed largely of blood clot with strands of pale pink tissue through it and along the surface of the uterine muscle there was a well-defined zone of this tissue mixed with patches of blood, producing an appearance which suggested the site of attachment of a placenta. Microscopic examination showed this to be the growing zone of the tumour; further details are given in the histological report.

The contraction of the uterine muscle was very striking on laying

open the organ; it accounts for much of the pouting overhanging appearance of the tumour in Fig. 1.

The history is somewhat indefinite, but probably the symptoms of September 20th, 1900, which were those of threatened abortion, may be taken as the beginning of the case. As early as February, 1901, Dr. Edgar suspected that he had to deal with a case of deciduoma malignum; the subsequent good health lulled his suspicions, but he and Dr. Burges continued to watch the case. The operation was performed 12½ months after the first symptoms of abortion, and after about two months of renewed symptoms of uterine disease. After the operation, the patient made a good recovery and enjoyed good health until the 29th of May, 1902, when, while out for a walk, she had a sudden attack of giddiness.

After rest in bed the symptoms passed off, but on the 5th of June a similar attack occurred, in consequence of which Dr. Burges was consulted. As there were no definite symptoms the patient was placed on tonic treatment. She got quite well, but on the 25th of June had a sudden attack of frontal headache with severe retching and vomiting, which lasted all day. During the two following days the patient became worse, and on the evening of the 27th began to be drowsy, gradually passing into a condition of stupor. She gradually improved, and on the 3rd of July was quite bright and intelligent, and took food well, but on the following day the symptoms returned. On the 4th the pulse ran as high as 165; temperature rose to 102·5 F., and breathing was of the Cheyne-Stokes type. On the 5th the temperature reached 104·6, rapid action of the heart continued, and the patient looked moribund. On the 6th there was some improvement. On the 7th she was very much better, but on the 8th she again became drowsy. On the 11th she was quite unconscious. Vomiting occurred repeatedly, and she died on the 14th of July without recovering consciousness.

Dr. Edgar saw the patient on the 20th of June. The vaginal examination showed that there was no local recurrence of the tumour. The patient then looked fairly well and was able to speak to Dr. Edgar. Although the importance of obtaining a post-mortem examination was pointed out, the friends of the patient would not consent to its being made. The termination of the case then is decidedly unsatisfactory.

The occurrence of metastatic tumours in the brain has been determined in 13 cases; those of Jurassowsky, Inglis and Bruce, Busse, Marchand (two), E. Frankel, Gebhard, Scherer, Tibaldi, Krewer (two cases), Davis and Harris, and one of the cases which Professor Weichselbaum allowed me to examine. The symptoms have usually been rather indefinite. It seems, therefore, fairly probable that in this case the fatal result was due to secondary growths in the brain.

In the case of Inglis and Bruce, the cerebral tumours had the appearance of simple cerebral hæmorrhages and their connection with the uterine tumour was demonstrated only by the microscopical examination. In this case, and those reported by Marchand, the presence of deciduoma malignum was not suspected, but the patient died with symptoms pointing to the presence of a cerebral tumour, and the post-mortem examination demonstrated the actual nature of the disease.

From the point of view of treatment, the result is in so far satisfactory that she made a perfect recovery and enjoyed nine months of good health after the operation. The hæmoptysis which occurred after the operation was certainly of pulmonary origin and was regarded as probably indicating secondary infection of the lungs. Possibly the amount of manipulation of the tumour may have given rise to embolism, but beyond the sputum there was nothing to suggest this. The character of the sputum reported in several cases was similar.

Case 3. Dr. Munro Kerr's. To Dr. Kerr and Prof. Muir I have to offer thanks, not only for the specimen, but for much encouragement and for assistance in obtaining the literature of the subject.

Mrs. D., ætat 23, was admitted to the Western Infirmary on the 17th of May, 1902, suffering from pain in the abdomen and hæmorrhage from the uterus. There was a history of a miscarriage in the preceding September. In March she was curetted, but a definite history in regard to this was not obtained. After this she states that she suffered from pain in the abdomen and constant bleeding, and felt ill and feverish. On admission she appeared very ill. She was very anæmic. On the 23rd of May the uterus was cleared out with the curette and fingers. Several masses of what were regarded as placental tissue were removed and thrown away without being examined microscopically. Next day the temperature rose to 106 degrees F., but fell within 24 hours, and remained normal for about a month. Then it began to show an evening rise, on one occasion going as high as 105° F. Some septic condition was suspected, and intra-uterine douching was resorted to. It was followed by a very severe hæmorrhage. Deciduoma malignum was indeed suspected. On the 31st of July Dr. Munro Kerr, acting for Professor Murdoch Cameron, extirpated the uterus per vaginam. The preliminary examination provoked an extremely violent hæmorrhage. The patient appeared almost moribund, but the operation was gone on with and the uterus removed as rapidly as possible. She died later in the day. *Post-mortem* examination was not allowed, and it is therefore impossible to state whether metastasis had occurred. Some hard cords were felt in the vagina which suggested secondary tumour, but it was impossible to examine them properly at the time of the operation. The total duration of the case was 10 months.

The tumour is almost identical with that from the preceding case. It is not quite so large and it is situated towards the right side

of the uterus, covering the orifice of that tube. The histological appearances in these two tumours are also very similar. Both of them show all the characteristic cell forms, and owing to the favourable circumstances in which they were obtained, the fixation of the material for histological examination is perfect. The relative amount of syncytium and Langhans' layer cells and of infiltration, and the large sarcoma-like cells varied in different parts of the tumour. The histological description which follows is largely founded on these two tumours. In neither of them were villi present. Sections of the old case and a number of preparations given to me by Professors Marchand and Veit, Drs. Schmorl and Haultain, also have been used freely.

The uterine mucous membrane in Dr. Edgar's case in part had the appearance of an ulcerating surface with few remains of glands in its deeper parts. Probably this was the area which had been traversed by the curette on the 25th of September. In the area which was overhung by the tumour, the surface epithelium was well preserved and many of the deeper cells had the character of young decidua cells. The mucous membrane covering the surface of the tumour was deeply eroded and in parts reduced to a mere layer of granulation tissue or necrosed tissue and fibrin. I did not find the conversion of the uterine gland or surface epithelium into syncytium, such as Gebhard and Marchand have observed in one or two of their cases. These two cases belong to the somewhat slow going type, contrasting with the first, which is a typical example of the rapidly fatal tumour which originally attracted the attention of Sänger and the other early observers of this disease.

Case III. Dr. Elizabeth Pace's. This case, as already mentioned, must be regarded as a doubtful one, but it is of special interest as being one of the connecting links between deciduoma malignum and the hydatidiform mole. No regular case of destructive hydatidiform mole has, as yet, been recorded with proper histological details in Britain; that of Champneys appears to have been of this nature, and one of the oldest cases is the classic one of Wilton. The connection of the tumour with the chorionic villi has been directly demonstrated in this country in the case of Haultain, one of Prowse's cases (as yet unpublished), and less definitely in the case of Inglis and Bruce.

The case of Dr. Haultain—

This was a typical example of deciduoma malignum in which a few villi were present. Hæmorrhage commenced 3½ hours after the expulsion of a hydatidiform mole. A few days later a large fibrinous mass "not

unlike a carneous mole" was expelled. Along with this there was severe hæmorrhage, sub-involution was suspected, and the uterus was cleared out by Dr. Haultain. The hæmorrhage which accompanied this was so violent that deciduoma malignum was suspected, and the material was kept for microscopical examination, with the result that deciduoma malignum was definitely diagnosed one month after the abortion. As the patient had improved greatly within the few days between the curetting and the diagnosis from microscopical examination she refused further operation, but seven weeks later a hæmorrhage occurred which was almost fatal. After allowing three days for the patient to recover somewhat Dr. Haultain extirpated the uterus per vaginam. The tumour was a small one, and consisted of blood clot and a few villi showing the enormous proliferation of the epithelium, which is shown in figures 8 and 8a, and the characteristic infiltration of the uterine muscle and the invasion of the blood-vessels.

Clinically and histologically, there cannot be the slightest doubt of the malignancy of this case, but, thanks to the early operation, the patient made a good recovery, and is still alive and well. If Dr. Pace's case be excepted, this and Lewers' case are the only British ones with a favourable termination. I have to thank Dr. Haultain for permission to use the figures, which are taken from his specimens.

History of Case No. 3. Dr. Pace's.

Mrs. McA., aged 23, two children, was admitted to the Victoria Infirmary under the care of Mr. Maylard on October 31st, 1900, as an urgent case of hæmmorhage following the expulsion of a large hydatidiform mole. At the end of July, 1900, while still nursing the youngest child, the patient noticed a little red discharge from the vagina, which she regarded as a return of menstruation. During August she had occasional slight bleeding with a certain amount of pain. In September the bleeding became more severe. On October 30th labour came on with severe bleeding, and a vesicular mole was expelled. The vagina was plugged by Dr. Weir, and the patient sent into hospital.

On the 31st the plug was removed and the uterus douched out. A considerable red discharge mixed with shreds of tissue continued until the 6th of November, when the patient was examined under an anæsthetic. At this time she appeared fairly well nourished, but was very anæmic. The uterus was enlarged and could just be felt above the pubis. The fundus felt somewhat thin. On the anterior wall were masses of soft tissue which broke off readily. The cavity was cleared out as thoroughly as possible with the finger by Dr. Pace, douched and plugged with iodoform gauze. There was very little bleeding. The right ovary could be felt to be cystic and about the size of a walnut. The left ovary was not felt.

The same evening the patient had a rigor, the temperature rose to 104° F. The gauze was removed and the uterus douched out. The temperature came down at once and remained normal until the patient was sent to the Convalescent Home on the 17th of November. There had been no red discharge since the 6th, and the uterus had diminished very much in size. Dr. Anderson, Pathologist to the Hospital, reported on the 10th of November that the tissues removed were typical hydatidiform mole.

On the 1st of December, *i.e.*, 32 days from the abortion, a bad flooding occurred, which was checked by rest, hot douching and ergot. On the 10th there was a little bloody discharge which continued, and on the 11th and 14th there were hæmorrhages of an alarming character. On the 15th the patient was brought back to the Victoria Infirmary. The temperature, on admission, was 102·4° F. On the 16th, under an anæsthetic, the cervix was dilated with Hegar's dilators. The examining finger came upon small soft projections, especially in the left cornu; some fleshy pieces were scraped out with the finger. Some of these were as large as peas. There was not much bleeding. The uterus was thoroughly scraped, washed out with boracic acid and plugged with iodoform gauze. The uterine wall in the region of the left cornu during the operation was felt to be thin. For three days the temperature remained above 101°. On December 19th it fell to normal, and remained so.

Dr. Anderson reported that the scrapings showed sarcoma-like elements and epithelial cells which suggested deciduoma malignum. Comparison with sections from Dr. Kelly's tumour strengthened this impression. The patient was extremely weak and anæmic, but as she appeared to be improving it was decided not to perform any radical operation immediately. But before allowing her to leave the Infirmary a thorough examination was to be made, and she was to be kept under observation.

On the 8th of January, 1901, 71 days from the abortion and 23 days from the last curetting, this was undertaken. She was prepared for operation if that should be considered necessary. There was no discharge from the uterus, which was found to be smaller than on last examination, but still somewhat enlarged. The sound on being introduced passed without encountering any but the very slightest resistance for an unusual distance into the abdomen, and was felt presenting against the abdominal parietes. Perforation of the uterus in the left cornual region was diagnosed. Vaginal hysterectomy was at once performed; the ovaries and tubes were removed along with the uterus. The patient made a slow but complete recovery. She reported herself in December, 1901, being then in good health. Some time later pulmonary symptoms developed which were regarded with suspicion and recurrence was feared, but they disappeared, and she reported herself recently in good health.

The uterus was expected to reveal on examination deep erosion by a malignant ulcer. Actually it was a very soft, flabby, slightly enlarged organ, which on being slit open showed no tumour, but only an appearance of having been somewhat recently thoroughly curetted. The sound had passed through in the left cornu quite close to the orifice of the Fallopian tube. Sections were prepared from several places, including the seat of puncture. At the last point nothing resembling tumour could be seen, but there was an area over which the wall was abnormally thin. Owing to the method of preparation the presence of fatty degeneration could not be properly investigated, but the muscle was very soft, brittle and pale. In one series of sections from a part of the anterior wall, which to the naked eye suggested the placental site, were found a few syncytial masses embedded in the remains of mucous membrane, and one or two which had even penetrated in amongst the muscle, and one or two lay free in blood-vessels. The muscle was almost completely denuded of mucous membrane. There was some superficial round-celled infiltration. Nothing else abnormal could be found.

The case was handed over to me for investigation along with that

of Dr. Edgar, Dr. Pace supplying the clinical particulars, and Dr. Anderson giving me his sections, and what remained of the curettings of the uterus. From Dr. Weir I received the mole. All the tissues had been preserved in formalin solution.

The last was a typical hydatidiform mole of large size and very much torn. Part of it had a covering of decidua which was very ragged. Sections prepared from several different parts showed that the greater part of the villi were necrosed and embedded in blood-clot. Others, however, showed the typical structure of vesicular mole, the epithelium of some of the villi being considerably hypertrophied in places, both layers participating, but the overgrowth was no greater than, nor in any way different from, that seen in several specimens of innocent hydatidiform mole with which it was compared.

In the sections of the curettings removed on the 16th of December, on which Dr. Anderson had founded his diagnosis, there were a number of villi, some of which were slightly hydatidiform whilst others were, as regards their mesoblastic cores, quite normal. Most of them showed very marked hypertrophy of the epithelium, and in some of the syncytium and masses of Langhans' layer cells there were nuclei of very large size. Here and there in the connective tissue of the villi were large cells similar to the syncytial wandering cells—the so-called "Neumann's cells." The shreds of mucous membrane did not show the characters of decidua; one or two of the portions included uterine muscle. In the mucous membrane there were no epithelial wandering cells, but the shreds of muscle showed infiltration by these cells in considerable number. With the experience which I then had, I would have agreed with Dr. Anderson in regarding the case as probably deciduoma malignum of the variety containing a few villi, and I would have advised extirpation of the uterus. The clinical indications also pointed in this direction.

Cases of repeated hæmorrhage after abortion or hydatidiform mole, leading to anæmia and loss of health, are not uncommon, and these symptoms usually disappear after the retained placental tissues have been removed. In this case, a thorough clearing out of the uterus had been done seven days after the birth of the mole. The patient had been much reduced by the repeated oozing of blood prior to the birth of the mole, and the severe hæmorrhage which accompanied it, and she improved considerably after this operation. Twenty-five days later, there was a flooding which was repeated three times within the next fortnight, and was so severe as to be alarming. The patient became extremely weak and was of a yellowish pallor

suggestive of pernicious anæmia or cancerous cachexia. The examination of the uterus revealed considerable enlargement and in its cavity was a soft friable protuberance resembling tumour tissue. All this strongly pointed to malignant disease.

Now, in the light of what was shewn to me on the Continent, and further study of hydatidiform moles recorded in the literature of deciduoma malignum, I would not care to give such a confident opinion. It is clear that one must be most careful in dealing with all cases in which villi are present. Repeatedly it was demonstrated to me that curetting after a simple hydatidiform mole may bring to light villi which are very little different from those found in the fatal malignant moles. It seems at present impossible to draw a sharp distinction between the simple moles and the malignant moles and chorionepitheliomata, either in respect of their early clinical history or the histological appearances. With a history so suggestive and considering also the undoubted danger of peritonitis after perforation with the sound, there can be no doubt that the immediate removal of the uterus was the right course to adopt. Had this accident not occurred, the comparatively small size of the organ and the absence of discharge, and the slight improvement which the patient had shown would probably have determined Dr. Pace in the policy of delay.

The history of the malignant cases shows that the uterus fills up again very rapidly after curetting. For example, in Dr. Edgar's case it was as large as ever within 20 days; in that of Von Franque in 12 days. In the Hartman and Toupet case, the symptoms recurred within eight days, and in Graefe's the tumour reached the size of a hen's egg in a month. On the other hand, there are cases in which curetting has been followed by a long period of quiescence suddenly broken by the reappearance of malignant symptoms, rapid development of a tumour in the uterus, metastasis, and a fatal result, *e.g.*, in Butz's case the interval of quiescence was nearly a year with regular menstruation, yet she died just a year after the curetting. (Compare also the cases of Klien and Krebs.)

The condition of the uterus here by no means proves that operation was unnecessary. The presence of masses of syncytium shows that chorionic remains were present which might have developed into a tumour. Whether, apart from malignant disease, such cells would be found 71 days after the removal of the mole and 65 days after thorough clearing out with curette and fingers, is a question to which no definite answer can, I think, be given. Villi, however, it must be remembered, were present 23 days before the radical

operation. In a case of vesicular mole which proved to be innocent, Poten and Vassmer found similar cells in the uterine muscle removed with the curette 52 days after manual clearing out.

Probably, therefore, less importance should be attached to those few portions of syncytium than to the clinical history of the case and the report on the second curettings. It is a serious matter to castrate a young married woman, yet when the whole history of the case is taken and compared with those of fatal deciduomata, and when the good subsequent state of the patient is considered, I cannot but feel that the accident was not altogether an unfortunate one.

A similar accident occurred in the case of Marchand (Everke), and in the cases of Menzel and V. Fleischmann, the Recamier blunt spoon was pushed through the diseased uterine wall. In the deciduomata of Gottschalk, Aczel, Reinicke, and the malignant moles of Wilton and Gottschall, spontaneous rupture of the uterus in consequence of deep ulceration by the tumour occurred.

The case of Menzel is particularly apropos.

A woman of 23 years had four full-time children in four years. All the confinements were perfectly normal. Three weeks after the last irregular hæmorrhages set in, and she wasted rapidly and became intensely anæmic. Six weeks after the confinement she applied for treatment. The uterus was one and a half times its normal size, and of very soft consistence. There was a bloody, slimy discharge. The first impression was retention of placental tissue and sub-involution. Next day the os was dilated and the cavity of the uterus explored with the finger. In the fundus, towards the insertion of the right Fallopian tube, was felt a ragged depression in the wall which admitted the finger tip. Bimanually the wall could be felt to be thin, and palpation was painful. As the finger-nail failed to detach pieces for microscopic examination the Recamier curette was very cautiously applied. Suddenly it perforated the thin spot. It was immediately withdrawn. The uterus was not washed out—simply packed with iodoform gauze. No particular bleeding nor fever followed. Microscopic examination showed the tissues characteristic of deciduoma malignum. In consequence of this report the uterus and appendages were removed next day. Patient made an uninterrupted recovery. Eight months later she was seen again. Her condition had improved vastly and there were no unfavourable indications. The microscopic examination of the uterus showed that the depression was a deep chorionepitheliomatous ulcer. The rest of the uterine cavity was already clothed with regenerated mucous membrane. The muscle was soft and showed among the cells spaces filled partly with loose connective tissue, partly with young connective tissue and numerous blood-vessels, a condition resembling that described by Guérard (*Cent. für Gyn.*, 1901, p. 1,138) in two cases of perforation as myometritis with hyaline degeneration.

Menzel remarks that an examination of the literature of the last 15 years shows that perforation of the uterus is no rarity, and that nearly every busy gynæcologist will have had the experience. With

proper treatment it seldom gives any trouble or necessitates extirpation. The warning as to the dangers of the curette is given in every text-book, yet the accident occurs in the hands of the most skilful and cautious. Menzel concludes that in most of such cases the blame should rest, not on the operator who has taken all reasonable care, nor on the instrument which must often be used, but on the tendency of the uterus under certain conditions to be extraordinarily soft and brittle. Of these conditions the process of involution after pregnancy is a common one and deciduoma malignum a comparatively rare one. But is is far from being a negligable one.

Histological Details.

Methods. The specimens in cases Nos. 1 and 2 were obtained immediately after the operations. Portions were at once cut out and fixed in corrosive sublimate-acetic acid fluid, and from case 2 in absolute alcohol and Herman's platinum-osmium-acetic fluid also. The whole uterus was then placed in formalin and salt fluid for conversion into a museum preparation. Sections were also prepared from portions treated in this way, and the fixation of these was found to be tolerably good. Various processes of staining were tried, the most satisfactory being hæmalum and eosin or hæmalum and Van Gieson for the sublimate, alcohol and formalin tissues. For those fixed in Herman's fluid iron hæmatoxylin gave particularly beautiful results. Saffranin and Lichtgrün were less satisfactory. Staining for glycogen was not successful as the alcohol fixed material was lost. The sections were cut by the paraffin process and complete series of considerable length were used.

The four cases which I have examined, while they all present certain special features which either have been referred to in the clinical reports or will be taken up later, correspond so closely in the general histological characters that one description will apply to all of them.

The tumour springs from a broad base and usually projects considerably into the cavity of the uterus. In the Kelly and Teacher, and the Edgar cases, there is an overhanging portion projecting into the lower part of the cavity. Into this the muscle seems to be drawn up to some extent, Fig. 2. The greater part of the tumour mass in section is of a dull red colour, fairly uniform in texture and looks like old blood-clot; microscopic examination shows that it is, in fact, of this nature, but mixed with remains of uterine tissues, and tumour tissue in a state of necrosis. Practically all the central parts of the growth are in this state. Nearer the uterine muscle, the tumour presents a patchy red and white appearance, suggesting placental site in section. This zone consists of tumour masses, some actively growing, others more or less necrotic, mixed with areas of

blood which simulate the uterine sinuses. The actual growing tumour for the most part lies between this layer and the uterine tissues and may be seen in places as a somewhat irregular layer of tissue one to two mm. broad, which is just distinguishable from the muscle by being of a whiter and less shining appearance. This distinction is too delicate to be properly appreciable in the figure. The nature of these layers was determined by the microscopic examination.

With a low power it is found that outrunners of the tumour burrow deeply into the muscle, especially along the tracks of the blood vessels, loosening it out and pushing layers of it up into the body of the tumour. This may give rise to a somewhat alveolar arrangement of the tumour (Fig. 6), but it is quite irregular and coarse, and totally different from the typical alveolar structure characteristic of carcinoma. The tumour does not contain connective tissue stroma or blood-vessels of its own. Like its physiological prototype it is a parasite on the maternal tissues and depends for its life on the maternal blood. Masses of the sort shown in Fig. 6 may be found deep in the muscle quite separate from the main tumour and are, in fact, metastatic tumours. This was recognised in case i., but not in case ii. Fig. 15 represents a section of one of the burrowing processes in the course of a blood vessel; the wall of which was almost completely replaced by tumour. A less advanced stage of this is seen in Fig. 12; a small metastasis in Fig. 16.

Many of the difficulties that have arisen in the interpretation of these tumours are due to the variety of cell forms which occur. Some of the appearances are due to degenerative changes leading up to necrosis. Others correspond to what is seen in the placenta, and is presumably physiological there; others, again, may be an expression of the intense activity of the malignant growth. Between these classes of changes in the typical cells, it is not easy to make a sharp distinction.

Fig. 6 shows most of the types of cell formation under a low magnification. In this, which was taken from a preparation stained with iron hæmatoxylin, the uterine muscle of a lighter colour and showing only small nuclei and a decidedly fibrous appearance is seen above and to the left. The darker masses are the tumour which in this place is infiltrating the uterine tissues principally in large masses, giving rise to the irregular alveolar arrangement already referred to. Fig. 7 shows a part of the regular layer of tumour forming the floor, as it were, of the malignant ulcer taken from about

the middle of the growth. In both figures it will be seen that there are two principal cell forms.

(1) The syncytium (syncytia or plasmodia); large multi-nucleated masses of protoplasm of various shapes and sizes, rounded or oval giant cells, long drawn out bands and whorls and quite irregular sprawling masses. These are frequently riddled with vacuoles which may contain *fluid blood* and which frequently spin it out into meshworks of very fine threads. (Figs. 11 & 20.) The nuclei are generally small, oval, dense, and stain uniformly and deeply with the ordinary chromatin stain, therein corresponding with the syncytium which is seen in the normal placenta; but not infrequently nuclei of other types are seen in the syncytium; especially there occur large clear and vesicular ones with well-marked intra-nuclear network and one or more nucleoli, and showing a comparatively light staining appearance. (Figs. 15 and 16.) Karyokinetic figures do not occur, but appearances suggestive of direct division are to be found. The protoplasm typically shows an opaque appearance and stains deeply with eosin and other plasma stains. The depth of staining varies considerably. The differentiation of the syncytium from the other leading cell form is particularly well brought out by hæmalum and Van Gieson's solution. With this combination the colour of the cytoplasm varies from a deep green through lighter shades of green to yellow, drab and brown. The lighter shades of green are characteristic of tissue which, to judge by the regular oval fleshy vesicular nuclei, are young and active. It distinguishes, further, the outrunners of syncytium which are found in considerable number infiltrating the adjacent muscle, and differentiates them sharply from the muscle fibres which are stained of a pure yellow colour. (Figs. 6 and 7.) The syncytial masses undergoing necrosis may be of a very dark green colour, or they may show more or less of yellow (in some cases brownish); in the advanced stages a pure yellow colour very similar to that which the muscle fibres show. The nuclei in this condition are small, shrunken, indented, and deeply staining (pyknotic nuclei). Such cells are frequently loaded with fat globules; this appears to be fatty degeneration, though sometimes it is seen in healthy-looking masses, and may there represent the physiological fat of the normal syncytium.

Examined with an oil immersion objective, the cytoplasm seems to have the structure of a sponge work or foam (alveolar structure). This varies greatly in its distinctness; in the younger masses the protoplasm is so opaque and uniform that it cannot be made out, while in those which are older, and especially some of the much vacuolated masses, it is quite a coarse sponge work. (Fig. 21.) This is totally different from, and independent of, the vacuolation. An appearance which is frequently observed is that along the borders of hæmorrhages, where the tissue had been pushed aside and stretched the meshwork is drawn out so as to simulate the longitudinal fibrillation of the muscle cells, but it is far less fine and delicate, and wants the regularity which these present. Some of the syncytial masses among the muscle are very fine and long drawn out, and through being of somewhat pale colour present an appearance which could give rise to the impression that they are modified muscle cells. The origin of sarcoma cells from uterine muscle is well known, and doubtless it was appearances such as those described above that led Menge, and recently K. Winkler, to regard the deciduoma as a sarcoma originating from uterine muscle. Whittridge Williams, who was one of the first to trace this origin of sarcoma cells, also was at first inclined to regard his

tumour as a sarcoma originating from the uterine muscle, and did describe it as such in his preliminary note, but subsequently recognised and pointed out this error. Isolated mono-nucleated cells with protoplasm identical with that of the syncytium are also seen. These will be discussed later.

I have been able to trace in the normal placenta or in hydatidiform mole which did not give rise to a malignant growth most of the modifications of syncytium which were observed in the tumour. The large vesicular nuclei in the syncytium must be regarded as an evidence of extreme activity, and in a question of diagnosis I would regard them as abnormal. They cannot be regarded as a sure sign of malignancy for they are seen in innocent hydatidiform mole and in young trophoblast of ova such as those of Peters and Siegenbeek van Heukelom. The so-called "ciliated" border is frequently very beautifully shown in the tumours. (Fig. 17.)

(2) Individual well-defined mono-nucleated cells which in a case containing villi are seen to be derived from the Langhans' layer. (Figs. 8, 8a and 9.) These usually form masses of some size intimately united with the syncytium. The regular relationship which is seen on the villi where the syncytium forms a thin layer enclosing the individual cells is also observed in the tumour, but in general the relationship between the two is irregular; it is an exaggeration of what is seen in the cell knots and epithelial expansions at the attachment of villi to the decidua. Where the tumour is in contact with the maternal tissues the syncytium, just as in the placenta, appears at the sides of the cell masses, and the individual cells are seen in actual contact with muscle or whatever the tissue may be, and even to some extent infiltrating it. (Figs. 12, 13, 14.) The syncytium may form a mere endothelium-like edge to the cell masses or it may be a broad border and also send in irregular processes among the individual cells. (Figs. 6, 7, 10, 11, etc.) Remains of connective tissue amidst the tumour cells as fine shreds of a bright red colour are frequently to be seen. (Fig. 22, photo.)

The individual cells in the youngest stage are small, polyhedral in shape, and closely packed together. Fig. 8 shows at once their source of origin and their character. The nuclei are round or oval, clear, vesicular, with well-marked intra-nuclear network, large nucleoli, and stain moderately deeply. Relatively to the cell-body they are very large. The cytoplasm with a low power is clearer than that of the syncytium, and does not stain readily with eosin. In a hæmalum and Van Gieson preparation it has a somewhat greenish grey colour and is not very clear. With a high power the opacity is found to be due to the presence of a darkly-staining fine close reticulum; this is quite unlike the alveolar structure of the syncytium. The older cells are clearer and larger, and their edges are sharply defined; in the way they are packed together they are characteristically epithelial cells. The reticulum is opener and less deeply stained; the nuclei are larger, but the cell bodies are relatively still more enlarged. Multiplication is by karyokinesis. The karyokinetic figures are perfectly regular, and multiple mitoses were not observed. Their number varies greatly in different fields; in fig. 8 they are numerous. The cells in division are large and clear, the reticulum is very open and looks at first sight as if retracted from the figure; actually in this part of the cell it is so fine as to be almost invisible. (Fig. 19.)

(3) There are, also, large cells of very varied shapes and sizes which do not conform to either of the types already mentioned. They are large cells,

and contain from 1 or 2 to 10 or more nuclei. They occur under two conditions:—

(*a*) In masses which in the section are either attached to the uterine wall or may appear as if lying detached amid the blood (fluid or clotted), or they may be imbedded in fibrin. (Fig. 10.)

(*b*) Infiltrating the maternal tissues. (Figs. 12, 13, 14, 22.)

These are the cells which have given rise to most of the differences of opinion in the interpretation of the tumour, and their origin and relations have been described *ad nauseam*. The continuity of them with the first two classes of cells of the ordinary tumours and with the epithelium of the villi in the cases in which these are present is plain. They correspond to the cell knots and the expansions at the tips of villi; and the infiltrating epithelial wandering cells, which, over and above the regular syncytial wandering cells, have been referred to in section 3. (Figs. 3 and 4.) But the variety of cell forms and the degree of infiltration of uterine tissue is far greater than can be seen in ordinary preparations of the placenta. In the masses of hypertrophied epithelium of innocent hydatidiform mole the variety of cell forms is more closely paralleled, so that a sharp line of distinction on these grounds is impossible. The relationship to adjacent tissues is also an exaggeration of what can be found in the normal placenta. There they are usually shut off from the decidua by the canalised fibrin layer (figs. 4 and 4a), or if they are infiltrating it the degree of infiltration is small. (Fig. 4a.) They may be found at the mouths of blood-vessels attached to their walls or even under the endothelium. I have not seen cells of this class deep in the uterine wall, only the wandering masses of syncytium passing beyond the layer of decidua cells.

In the hydatidiform moles which have been examined in situ, however, an increased amount of infiltration is characteristic; so that here again no sharp line can be drawn. Cells of all sorts which can be traced to the chorionic epithelium are found deep in the decidua and even well in among the muscle.

In case 1 quite typical decidua cells were found near the border of the tumour where the overhanging edge had protected the mucous membrane from the curette. There were no tumour elements in the decidual tissue.

Along the edge of the tumour the maternal tissues show a certain amount of inflammatory reaction. The blood, both in the vessels and extravasated among the tumour, whether fluid or clotted, contains a high proportion of leucocytes, principally polymorphonuclear. Many cells of this class are seen in among the tumour cells (of all sorts), and many of them are seen actually within tumour cells; these frequently lie in vacuoles and present degenerative appearances, *i.e.*, the syncytium and the large cells at present under consideration show phagocytic properties.

The invaded maternal tissues may be uterine muscle or connective tissues or blood-vessel walls. Masses of tumour cells among the muscle fibres are not infrequently seen; occasionally tumour cells appear to be actually embedded in the muscle substance; but for the most part the muscle in the immediate neighbourhood of the tumour has atrophied and disappeared before the invaders reached it in any number. The tumour cells therefore lie principally in connective tissue, which may have a ragged eroded appearance and show hyaline degeneration, or may have been converted into granulation tissue. The former is represented in fig. 22, where shreds of connective tissue without many nuclei and rather

hyaline in character are seen permeated by the tumour elements. The granulation tissue character is seen in fig. 13.

In such places the tumour has quite the look of an infiltrating sarcoma, but the character changes at once when it is followed back to the cell mass; there is no trace of connective tissue stroma among the cells there, and no blood-vessels.

The mixture of cells in the infiltration zone is a very complex one. (Fig. 12.) By the exercise of diligence one could construct an unbroken series of intermediate forms between the huge tumour cells and almost any of the neighbouring tissues, mesoblastic or epiblastic, and found thereon a theory of origin, but such a process is not comparable with the obvious continuity between the typical tumour masses and the infiltrating elements. Figs. 6, 7, 13, 14.) The resemblance to decidua cells is slight. On the other hand, the same tissue which develops into decidua when it becomes the seat of a sarcoma shows elements not unlike the chorio-epithelioma, but the resemblance is only to the one part of it; when the whole is considered the tumours are utterly different. The photographs on pl. VI. show the differences between decidua and the infiltrating tumour better than any description. (See also section 6.) The nuclei of the decidua cells are much paler than those of the tumour cells, the intra-nuclear network is less developed, and they are smaller, both actually and, still more, relatively, to the cell bodies. The cytoplasm of the decidua cells of tumour No. 1 is very similar to that of the clear individual cells; the recticulum is very delicate; it had not attained the closeness and opacity seen in older decidua cells. Both classes of cells are described as containing glycogen. I was not able to investigate this. There is no fat in the decidua cells, whereas many of the others contain a few minute globules of it. Apart from these differences in details the general look of the two tissues is quite different. The decidua cells also plainly arise out of the connective tissue corpuscles. The typical small Langhans' layer cell is usually confined to the cell masses. All the infiltrating cells are more or less enlarged. Many of them are exactly like the larger clear well-defined derivatives of this layer in the cell masses, but karyokinetic figures in the zone of infiltration are rare, and for the most part the cells are much larger still. It is as if the cells invading the maternal tissues had laid aside their reproductive faculties and taken on an exaggerated vegetative growth. Thus many of the mono-nuclear cells are of very large size, six or seven times that of the parent cell, and have correspondingly large nuclei which may contain a very large amount of chromatin. The contrast between these cells and the leucocytes in figs. 10 and 12 indicates their enormous size better than any measurements. In many of them again the nucleus has divided, and the cytoplasm also shows changes in the direction of that characteristic of the syncytium. Lastly, many of the infiltrating cells are typical syncytium. These changes are better appreciated in the cell masses where there is no interstitial tissue to complicate the picture.

Fig. 10 shows a typical mass of these large cells. None of the smallest Langhans' layer cells appeared in the field drawn; but they are seen just outside of it; at the lower part are several of the somewhat enlarged ones. In the centre is a giant cell containing eleven nuclei in a clump in the centre; other cells in the mass contain two or three nuclei. With increase in size of the cells there is also a change in the character of the cytoplasm; the reticulum becomes closer and more opaque, and also changes from the grey tint of the typical Langhans' layer cell to light green or greenish

yellow. Karyokinetic figures are rare in these large cells, but I have seen typical examples of them alongside cells of similar character which contained two or more nuclei. I regard this as evidence of direct and indirect nuclear division occurring side by side in cells of common stock which are diverging into different lines of growth. Sharply contrasting with these cells are the dark processes and masses of syncytium seen in the figure, but in other similar cell nodules further stages intermediate between the giant cell in the centre and the dark green alveolar vacuolated syncytium shown in fig. 10 can be readily found. (Fig. 20.) This progression is less easily followed than that from the Langhans' layer cell into the giant cell, because the intermediate forms are not to be found all in the one clump of cells. The continuity of the series is, however, very plain.

Besides the forms of intermediate character individual cells with one or two or more nuclei and dark cytoplasm typically of the syncytial order have already been mentioned; these are seen here and there in free masses as well as infiltrating. Their relations to the syncytium are not always that of cross sections of bands, as Williams originally supposed. They appear to be produced by the giving off of numbers of very small syncytial buds—a direct proliferation and breaking up of the syncytium.

Among all these forms, then, one arrives at the position of other observers, viz., that it is impossible to tell where Langhans' layer ends and syncytium begins. Whether it is legitimate to regard this as homologous with the process of development of the syncytium out of the primitive individual cells as it occurs in the normal placenta or the trophoblast, or whether it is a peculiarity of the tumour, is another matter. It my opinion the problem of the formation of the syncytium is the problem of the origin of giant cells in general, and the evidence of the tumours has some value.

Long before Fränkel stated his conclusions that many tissues of the human body were inclined to form syncytium (or take on a syncytial form) besides the chorionic epithelium, this was a vexed question of histology. His statement is quite a valid one, but the conditions under which, and the steps by which, syncytium formation occurs are obscure. Peters sees in the trophoblast of his ovum all the intermediate cell forms (p. 48 of his monograph); they are plainer there than in any other normal trophoblast I have seen; his conclusion that the individual cells adjacent to the chorionic mesoblast are the primitive type out of which all the other forms arise has been mentioned: I hold it justified.

I am aware that Professor Peters is engaged on a fresh cell study of the re-stained preparation; criticism of his original description might perhaps therefore be left to himself. I disagree with his suggestion that the syncytium originates by a flowing together of the outer layers of the individual cells of the trophoblast in contact with the maternal blood which he supposes to exert some corroding influence on the cells and to cause them to lose their distinct outlines

(p. 50). This would correspond to the formation of the symplasma in the maternal tissues round the guinea-pig ovum which von Spee describes and which appears to be a degenerative process; I see no evidence of such flowing together to form syncytium in my tumours.

On the contrary, the large cells of the tumour closely resemble the giant cells of the trophoblast of various animals, *e.g.*, Tarsius spectrum, the development of which by growth and nuclear multiplication of the primitive polyhedral cells of the trophoblast without division of the cell body can be followed in all its stages. I believe the development of the syncytium of the human placenta is a proliferative process and not a process of fusion of originally distinct cells. The giant cells then either spread themselves out round the individual cells, or the latter become invaginated into the former; either way the arrangement characteristic of the later stages of the placenta (human or tarsius) is attained. I look forward with interest to the results of Professor Peters' re-investigation.

Besides the breaking up of the syncytium into the individual cells already referred to, the differentiation of cells having the characteristics of Langhans' layer cells within the syncytium has been described by various observers.

It is supposed that a nucleus becomes surrounded by a clear space containing a delicate reticular cytoplasm and sharply defined from the syncytium. In my specimens such clear individual mono-nucleated cells completely surrounded by syncytium are frequently to be observed. Where this forms part of a tumour mass it is reasonable to infer that the explanation of the appearance is the invagination of Langhans' cell derivatives into the mass of sycytium. I was unable to satisfy myself that it occurred in pieces of syncytium which were quite detached. Fig. 17 is unfortunately from the end of a series. The free tumour cells in blood-vessels were almost always syncytium only. I did not find potential emboli containing both cell forms; but processes of tumour containing them which looked as if they might easily get detached are plentiful enough. The subject of fig. 16 proves that the masses of plain syncytium can attach themselves to the wall of a vessel and grow to some size. The small metastasis here figured was examined from end to end in a series of sections. That it has grown in situ is indicated by the fact that the branch of blood-vessel on either side of the mass is very much smaller than the dilatation in which it lies. It contains no individual cells, but, apart from that, it has quite the look of a commencing tumour. If it were so the endogenous formation of Langhans' layer cells from syncytium would be proved. I have to leave the matter open.

Probably only a few of the syncytial masses in the vessels ever become tumour nodules, the bulk of them disappearing like the deported syncytium and villi of the normal placenta. Many of them are in an advanced stage of fatty degeneration. Exactly similar

syncytial masses occur much more frequently in the immediate neighbourhood of the growing tumour lying not within blood vessels, but in the interstices of the tissue, yet the invasion of the lymphatics and the secondary infection by lymphatic glands is quite the exception in this form of tumour.

The relationships between the different cell forms in the tumour and in its physiological prototype then are as follows:—

(1) The primitive type from which they all originate is, of course, a mono-nucleated cell—the undifferentiated blastomere. In the differentiated trophoblast or chorionic epithelium it is represented by the individual or Langhans' layer cell. The syncytium develops out of these by growth of the cell and division (amitotic) of the nucleus without division of the cell body, *i.e.*, it arises by a proliferative process and not by the fusion of pre-existing distinct cells.

(2) Both the Langhans' layer elements and the syncytium have each an extensive power of growth into cells of their own type. They are thus in a sense capable of independent development, although they usually grow in intimate association. This is shown in the continuance of the syncytium after the disappearance of the Langhans' layer in the later months of pregnancy. Also the syncytium gives off buds which may be mono-nucleated or multi-nucleated, and preserve more or less exactly the cytoplasmic characters of the parent tissue (the wandering cells).

(3) A retrogression of syncytium into Langhans' cells possibly occurs by the differentiation within the former of clear cells which have the characters and mode of multiplication (mitotic) of the latter.

The degenerative changes are less interesting than the proliferative, yet they are important, for in a portion of tumour scooped out for diagnostic purposes, degenerated is fully more likely to be obtained than unaltered tissue.

The principal changes of this nature in the individual cells are retraction of the cytoplasm from the nucleus, crushing together of the cells producing an irregular spindle-shape, shrinking of the nucleus and loss of the distinct intra-nuclear structure. The cells may also become loosened out in other cases. In degeneration the distinction of the two layers becomes lost. The syncytium preserves its features longer; therefore if there is any living tissue it will probably be a mass of large cells of very various shapes and sizes up to the large syncytia. (Fig. 24.) The appearance suggests malignant growth of some sort at least, if not definitely chorionepithelioma.

The tumour appears to have a special affinity, on which some of its most characteristic features depend, for the blood-vessels. Several more or less distinct types of invasion of blood-vessels, which were all described by Marchand, are recognisable in my specimens.

(1) The tumour grows into the mouths of the uterine sinuses, attaches itself and invades them from within (fig. 12), just as the detached masses already referred to attach themselves.

(2) The advancing tumour attacks the vessel from without, destroying and replacing the wall. (Fig. 7.) When it reaches the endothelium the tumour cells tend to spread along just under it for some distance, so that the vessel may come to have the appearance of a tube of endothelium in a sheath of large tumour cells. (Figs. 13, 14 and 15.) Sometimes a plug of tumour regularly invaginates the endothelium into the lumen. The invaded blood-vessels (at least those attacked from within) dilate; this peculiarity is particularly striking in the vaginal metastases which are usually taken to be varicose veins; this is referred to in the summary of case Kelly and Teacher at the beginning of section 5. Finally, the endothelium disappears or gives way. When this occurs, on the one hand the tumour cells enter the vessels, and on the other extravasation of blood into the tumour takes place.

Marchand and other observers have attributed to the invading tumour elements a blood-clotting influence. Peters, on the other hand, believes rather that they have the power of preventing coagulation, a power which I attributed to them in 1898. Their action perhaps is not very different from that of the endothelium which they replace, or of the syncytium of the intervillous space. Probably the clotting or remaining fluid depends on the amount of blood which has been extravasated, and the amount of damage that has been done to the tissues into which it has escaped. In Fig. 13 there is a thrombus where the endothelium is just disappearing, but in other sections of this series there is clear evidence of extravasation having occurred, and further out in the tumour there has been clotting. There is also a shred of thrombus in Fig. 12. On the other hand there is no sign of it in Fig. 16, or in the vessels in the middle and at the top of fig. 7. An active power of hindering clotting, on the other hand, seems doubtful. The outlying masses of tumour are usually imbedded in clot or surrounded by a layer of fibrin. The same is seen in abortions where a large hæmorrhage into the placenta leads to clotting. Here, there has been a gross laceration of tissue, a lesion which is usually followed by clotting, no matter what tissues are concerned.

Whereas in the normal embedding of the ovum the vessels which are opened by the trophoblast or burst into it are only capillaries or very small veins, in the tumour veins of very considerable size may be seen with their walls completely destroyed. The thick-walled arteries as a general rule appear not to be much affected by the tumour. These relationships explain at once the violent hæmorrhages which are such a characteristic feature of the growth and the metastasis by the blood stream, and the tendency to degeneration and necrosis of the cells.

The Chorionepithelioma of Teratomata.

The fact that tumours identical with chorionepithelioma in structure do occur apart from pregnancy was first noted by Kanthack and Eden under the circumstances already referred to. But Schlagenhaufer cites two cases of "sarcoma of the testis" which occurred when chorionepithelioma was yet unknown. In the description of one of these Langhans compared the structure to the chorionic epithelium, and in the other the description by Malassez and Monod* is almost exactly that of chorionepithelioma.

By the kindness of Dr. Eden, I saw some of the specimens which he and Kanthack showed to the Committee of the Obstetrical Society of London; in my opinion "the secondary tumours in the liver and lymphatic gland" are histologically identical with secondary tumours from an ordinary chorionepithelioma. The primary tumour presents a very different appearance. The case, so far as I am aware, has never been reported in detail notwithstanding that it was one of the principal factors in bringing about the decision of the Society and its Committee. Indeed the occurrence of such tumours apart from pregnancy was the most telling point in the case of the opponents of the new views, and the only one which was not capable of explanation there and then.

Chorionepithelioma *in the uterus* apparently quite independent of pregnancy has also been observed by Lubarsch. The history is as follows:—

> An exploratory laparotomy in a girl of 13 years who had never menstruated revealed a large tumour, which appeared to grow from the uterus. Owing to widespread adhesions extirpation was not performed, but portions were removed. The growth to the naked eye, and still more on the microscopic investigation, resembled chorion-epithelioma so closely that Lubarsch described it as a "double" of that tumour. Before he knew the history of the specimen he had indeed no doubt that he was investigating a chorion-epithelioma. The patient was unfortunately taken away by her friends, and the case could not be fully investigated.

Schlagenhaufer remarks that "these are two concrete cases which with full knowledge of the chorionepitheliomatous tumours could be advanced as evidence on the one hand against the specific nature of these tumours, and on the other hand against the prevalent opinion that they originate from the epithelial covering of the chorion."

To them may be added a third, observed by Bock, in which a typical hydatidiform mole was passed by a virgin of $12\frac{1}{2}$ years.

* The first-named author was uncertain whether his tumour should be classed as a sarcoma or a carcinoma; the others termed their specimen a "sarcoma angioplastique" on account of the resemblance of some of the vacuolated syncytial masses to developing blood-vessels.

The patient, who had always enjoyed good health, menstruated for the first time at the age of 12 years and two months. The flow was moderate in quantity, contained some small clots, and was painless. With rest in bed it ceased after eight days. The second was accompanied by pains in the region of the kidneys and very little discharge. On the second day a clot enclosed in a whitish membrane was passed, and the pain then ceased, and the discharge flowed in a normal manner for four days. The third menstruation was also painful, and clots representing casts of the cavity of the uterus were passed. The fourth, still more painful, resulted in the passage, after three days, of a typical hydatidiform mole about the size of a walnut. It consisted of a circular membrane 3—4 mm. thick, about the size of a two-franc piece, from which hung a series of strings of vesicles varying in size from that of a pin-head to that of a pea. Dr. Bock informed me that there were 20 to 30 such strings. The specimen was apparently examined with the microscope in the fresh state only, and it is no longer in existence; but there appears to have been absolutely no doubt felt as to its nature. The patient has menstruated regularly and without trouble ever since. She is of good family, and her parents gave absolute guarantee that so far as careful surveillance was concerned she was a *virgo intacta*. The evidence from the physical examination and the circumstances of the case—the regular menstruation for the four months—also go against any idea of pregnancy having occurred. Bock suggested that the mole was a "fœtal inclusion."

Before taking up the cases of Schlagenhaufer the sense in which the term teratoma is used must be explained, as it bears a somewhat different significance in English and in German scientific writings. Bland Sutton reserves it for such tumours as clearly arise from the remains of an included fœtus.

German authors, of whom Marchand, Bonnet, and Wilms may be taken as representatives, use it in a much less restricted sense. The position is most briefly and systematically stated by Marchand.*

The symmetrically formed, but unequally developed, double monsters are excluded from the teratomata. There remain the true parasitic monsters—implantationes or inclusiones fœtales, in which the united Anlagen are in form, size and reciprocal relations quite unsymmetrical; the parasite is as a rule quite rudimentary, very irregularly developed, and quite dependent for its nourishment on the other (autosite). These are divided into two groups:—

(*a*) Intra-amniotic, including the parasites of the anterior end (epignathus), which are attached to the surface of the head, more rarely included within it, and the sacral teratomata.

(*b*) Extra-amniotic and enclosed by the closure of the body cavity, *i.e.*, within the thorax or abdomen (cœlom-parasit) or from there developed in the tissues of mesoblastic origin.

"To the fœtal inclusion are connected without sharp boundary line the so-called dermoid cysts which are commonly reckoned as tumours. Firstly, a distinction must be made between:

"(1) Those forms which arise through sequestration from the skin, and therefore consist of a simple sac clothed with skin, the walls of which

* *Vide* Literature list C.

occasionally contain cartilaginous, bony or glandular tissues; these are without difficulty explained as dislocations of rudiments of organs in the neighbourhood. Such are the dermoids one finds on the head and neck in the region of the primitive branchial clefts in the skull and in the mediastinum.

"(2) Dermoids or teratomata consisting of a complicated agglomeration of tissues which occur almost exclusively in the sexual organs, especially in the ovary, much less often in the testes."

Most of the tumours in the last class, Bland-Sutton would term dermoids, and would derive all their structures from pre-existing tissues of the person that bears them. Especially he lays stress on the fact that the predominating elements are epidermal structures, and he regards the tall columnar epithelium of the graafian follicle and the adjacent ovarian stroma as capable of giving rise to them all. On the other hand, Marchand, Bonnet and Wilms have demonstrated in these tumours representatives of all three embryonic layers. They regard them as representing a three-layered blastoderm (Keimanlage) which is formed after the fashion of a human fœtus; whereby the first differentiated tissues and organs, viz., the epiblastic ones and the head region come to predominate. They would be, then, "rudimentary ovarian parasites." The same hypothesis they apply to the solid mixed tumours of the ovary, and other organs. On it most at any rate of these complicated tumours originate not from the tissues of the organism which encloses them, but from some included cell which has the morphological value of a matured and fertilized ovum. Either at once (congenital tumours) or after an interval (mixed tumours of later life) this developes into an imperfect organism—a teratoma or embryoma.

Into their transcendental speculations as to the nature of this cell, it is not possible to enter more deeply here. The facts on which the theory is based can be found in the works cited. Nor can the interesting speculations of Dr. Beard of Edinburgh on the origin of tumours in general be considered.

In view of the ascertained facts, I regard the German classification of the whole series of tumours as the more logical, and the theory of origin as not less probable than that of Bland Sutton, with whom may be coupled Bandler. Both views contain a very large element of speculation.

In ovarian dermoids occasionally quite complicated structures have been seen in addition to nearly all the tissues of the human body—connective tissues, cartilage, bone, teeth, glands of various sorts, mammary gland, breast warts, fingers with nails, striated muscle, portions of central nervous system, pigmented epithelium identical

with that of the retina have all been observed in them. Occasionally dermoids of the ovary behave as malignant tumours. The mixed tumours of the kidney and testis have a bad reputation in this respect also. Malignancy of sacral teratomata is not unknown.

The tissue which behaves in this way may be sarcomatous or carcinomatous. In the malignant congenital sacral tumour observed in Glasgow by Coats, which I have re-examined in the hope of finding chorionepithelioma, a large part of the primary tumour and the secondary growths in the lumbar lymphatic glands present the characters of carcinoma. A remarkable tumour is the teratoma of the ovary described by Saxer (which he very kindly showed to me) in which the malignant growth was embryonic nervous (neuroepithel) tissue.

When so many structures can be found in these tumours, it is not surprising that chorionic tissues should occasionally occur. Nor is it surprising, in view of what we know of them in their normal seat, that being there they should manifest malignant activity.

Schlagenhaufer's first case:—

A man, of 43 years, from whom no account of his illness was obtained, died on 24th July, 1900. The diagnosis was left-sided pleurisy and pneumonia, possibly infarction of the lungs. The *post-mortem* diagnosis was sarcoma of the left testicle, with metastases in the left lung, thyroid gland, and right kidney. Perirenal hæmatoma from hæmorrhage in the renal metastasis and perforation of the capsule of the kidney.

The tumour, which was received after hardening in 5 per cent. formalin, was of roughly oval shape, measuring 11 by 8 cm. It was enclosed in a firm white connective tissue capsule, from which tense bands passed in, dividing it into several lobules. Testis and epididymis were recognisable to the naked eye. In section the tumour consisted of a brown-red crumbly tissue. Only in one more fibrous part were some little cysts to be seen, which were empty or contained a shining white material. It resembled, in fact, an ordinary uterine chorion-epithelioma after hardening. The pulmonary metastases were indistinguishable from secondary nodules of chorion-epithelioma in the lungs.

Schlagenhaufer's very clear description of the histological characters may be summed up so far as most of the primary tumour and the whole of the secondaries are concerned, as, *identical with those of chorionepithelioma to the last detail.* The relations of the two elements to the blood vessels were particularly clearly made out. The chorionepitheliomatous tissue and blood-clot made up most of the primary tumour, but the cells were well preserved in only a small

part of it.* In addition, the primary tumour contained at one part round the edge long-drawn-out flattened tubules lined with columnar epithelium one or two cells deep, evidently remains of the rete testis. Near these, but more into the middle of the tumour, were found ovaries with horny stratified epithelium and epithelial pearls. Dermal appendages were wanting. Larger cysts with cylindrical epithelium were also seen, and in one place tissues resembling embryonic lung, lymphatic follicle, young connective tissue and involuntary muscular fibre. Clearly, he says, we have to do with a teratoma of the testis; all three layers of the blastoderm and the trophoblast are represented. The enclosing albuginea and the testicular remains prove that it was a tumour of the testis itself. The secondary tumours on the other hand were pure chorionepitheliomata, the malignancy being confined to the representatives of the trophoblast (or chorionic epithelium). This corresponds to what is commonly seen in ordinary chorionepithelioma, where the metastatic growths are usually purely epithelial even when villi have been present in the primary.

In Schlagenhaufer's second group, not merely were there cells corresponding to the epithelium of chorionic villi, but there were also mesoblastic tissues—in fact, if the theory of origin be admitted, whole villi, mostly in a state of hydatidiform degeneration, and the case would be not inappropriately described as one of malignant hydatidiform mole in the male. He has collected five cases in which structures resembling hydatidiform mole in their naked eye characters have been found in the blood-vessels in connection with tumour of the testis. These were described as peculiar myxomata by Waldeyer and by Breus; as carcinoma by Kanthack and Pigg, as adeno-carcinoma myxomatodes by Silberstein, and as lymphendothelioma by MacCallum. Breus's case is that which Schlagenhaufer has re-examined. It had lain 20 years in 60 per cent. spirit and the microscopic preparations are therefore not good, but they are fairly distinct.

W. H., æt. 40, had noticed for six weeks a distinct and painful swelling of the scrotum, and complained of great difficulty of breathing and pains in the whole right side of the body. Examination showed a hard tumour of the right testicle; locally diminution of the pulmonary resonance and râles; cardiac area normal; weak apex beat; a loud double murmur at the

* This may be contrasted with Schmorl's case where the chorionepithelioma was found in a very small area only of the primary tumour although the secondary growths were very extensive, and with Wlassov's first, where out of ten large pieces he found it in only one. In the case of Schmorl the metastases in the liver had the appearance of pure chorionepithelioma, while those in the retroperitoneal lymphatic glands resembled carcinoma.

apex; tenderness of the lower part of the abdomen. The tumour increased in size very rapidly, and he died four weeks later.

The lungs were studded with secondary growths, some exactly like the secondaries in a case of chorion-epithelioma, others more like infarctions; the latter showed emboli consisting of plugs of the villous processes in the vessels supplying the areas. In the left auricle, hanging from the region of the fossa ovalis, a "gelatinous bunch of grapes-like new growth which might best be compared to the vegetations of a hydatidiform mole."

The testis and epididymis were easily shelled out of the scrotum; they formed a tumour about the size of a fist and consisted of a firm fibrous meshwork enclosing cysts. From the upper end of this stretched the thickened spermatic cord, the dilated veins of which were filled with long string-like growths that extended right up into the right auricle and through the foramen ovale into the above described mass. Nowhere was the growth adherent to the walls of the veins.

This condition is paralleled in the malignant mole of Solowij and Kryszkowski in which similar masses mixed with clot extended up the spermatic veins to the vena cava. MacCallum's case is extremely like Breus's; he described the intravascular growths as follows:—"These curious growths resemble nothing so much as the villi of the hydatidiform mole." Waldeyer also compared the growth in his case to hydatidiform mole.

MacCallum regarded his tumour as of endothelial origin. On the other hand, Schlagenhaufer not only could not trace the origin of his to endothelium, but he saw destruction of the blood-vessels just as in chorionepithelioma. The villous masses show the structure of hydatidiform chorionic villi including the characteristic two layered epithelium; but this was not made out without considerable difficulty owing to the bad preservation of most parts. Further, the manner in which the villi were pressed together in places resulted in an appearance like tubules lined with a peculiar epithelium embedded in a fibrous stroma; appearances which suggest a resemblance to that described by Wlassov. There were also real glandular tubules in these masses, which indicated their teratomatous nature. The occurrence of the whole of the chorionic villus is explained by the embryonal anlage having early gained access to the interior of veins, where the placental portions of it found space and suitable conditions for luxuriant growth.

Soon after the publication of Schlagenhaufer's paper appeared another by Wlassov in which four more tumours of similar nature were described. Wlassov came quite independently to the same conclusion, viz., that the tumours were teratomata. He takes, however, a different view of the origin of the chorionepitheliomatous tissue, which he believes he has traced to the epithelium of the glandular tubules in the tumour in two of his cases. Following the

strict theory of the teratoma, he would have regarded it as derived from an actual monstrous trophoblast, and did so at first. In his tumours there were no epiblastic structures, but only hypoblastic and mesoblastic were present. On this account, he considers the trophoblastic origin an unproved hypothesis. (This was writing without knowledge of Schlagenhaufer's work.) He sums up the tumour as an epithelioma *sui generis* of the testis developed out of the incompletely differentiated epithelium of embryonic gland tubules;—*not tubuli testis;—these he sees undergoing destruction.* The mesoblastic tissues are not the stroma of a carcinoma, but the product of the mesoblastic part of an embryonic anlage. They do not re-appear in the secondaries, which are composed only of the epithelial elements just as in the case of chorionepithelioma.

At Carlsbad, in connection with the demonstration of Schlagenhaufer, sections of another tumour of the testis were shown by Schmorl, and Bostrœm described a case in a male patient in which there were many secondary tumours resembling chorionepithelioma; in the latter case the primary tumour could not be identified; it was not testicular. It was also suggested that the case of Kleinhans, of chorionepithelioma in the ovary, might be of this nature, instead of an ovarian pregnancy. None of these cases has yet been published in detail.

Another testicular tumour of this class was shown to me by Marchand, but I am not aware that it has reached publication yet.* It has also been suggested that some of the tumours already described as chorionepitheliomata are of this nature; this might well be the case in such as that of Busse, vide Table I.

In the end of last year, L. Pick described a "cystic teratoma; so-called dermoid cyst" of the ovary in which "instead of chorionepitheliomatous tumour or metastatising hydatidiform mole was a hydatidiform-mole like growth of innocent type." Pick suggests that such tissue may occur in most of these tumours, but in such small amount that it had been overlooked.

Lastly, by permission of Dr. Ritchie, of Oxford, I am able to refer to a case which will be published shortly of malignant dermoid of the anterior mediastinum in a man.† In this case, a tumour of considerable size occupied the anterior mediastinum and the lungs were studded with large growths of typical chorionepitheliomatous

* Since this paper went to press this has appeared as an "Arbeit aus dem Pathologische Institut zu Leipzig," entitled "Uber das maligne Chorionepithelium und die analogen Wucherungen in Hodenteratomen," by W. Risel. 8vo., Hirzel: Leipzig. See addendum to Part II.

† See p. 65 of this Journal.

aspect. There were also many metastases in other organs. The primary tumour consists principally of tissue identical with chorion-epithelioma in which the Langhans' layer elements predominate. Cysts lined with horny stratified epithelium and containing hairs also occur and tissues of mesoblastic origin.

Probably we are only at the beginning of a controversy as to the nature of these curious structures, but in the meantime the view of Schlagenhaufer holds the field. The theory of Wlassov is no less open to objection than that of Schlagenhaufer, and against it is the fact that no exact imitation of the ordinary chorionepithelioma by tumour derived from glandular epithelium has yet been discovered. The histological details of Schmorl's tumour are not yet published, but the sections show gland tubules, and in the small area which is all that there is to represent the placental anlage there is something very like a gland tubule from which the tumour evidently is springing. (Fig. 26.) But the epithelium of this and the connective tissue below it resemble strongly a portion of a chorionic villus, and it is moreover something quite different from the glandular cysts around it which make up a large part of the section. Wlassov's photographs do not demonstrate to my satisfaction what they are supposed to do.*

In conclusion, then, I believe the view of Schlagenhaufer that these tumours are teratomata originating from some structure which has the morphological value of an included ovum, and the chorion-epitheliomatous tissues represent the actual trophoblast (chorionic epithelium) of the included ovum to be the most probable. In any case, the specificity of chorionepithelioma is not affected. The chorionic epithelium, as already remarked, is as characteristic a structure as any known to the histologist, and its specificity for the placenta is no more affected by the presence of it or of similar tissue in dermoid tumours of the testis or other organs than the specificity of hairs for the skin or teeth for the mouth, because they occasionally crop up in the rectum.

(To be continued.)

* Risel, like Wlassov, finds appearances which suggest that the chorionepitheliomatous tissue in teratomata develops out of gland tubules; but as he admits, the evidence is by no means conclusive. The tissue, he points out, is in all respects identical with chorionepithelioma and chorionic epithelium. He concludes, that it does not represent an anlage of the fœtal membranes, but is only one of many varieties of cell formation such as hairs, neural epithelium, etc., which the fœtal epiblast is capable of producing; further that there is no proof as yet that an anlage of the fœtal membranes can occur in a teratoma.

Why it should not do so as well as anlagen of hairs and teeth (or the fully formed structures themselves) is in view of the embryological facts not very clear to me. Risel's explanation of the hydatidiform mole-like structures in the case of Pick as deported villi from the tubal pregnancy which had been present, seems, in view of the facts of the case, rather far-fetched. In the case of Maydl (which as yet I know only at second hand) a teratoma in the abdomen in a male subject is described, which contained a well-formed trunk and limbs enclosed in an amnion a substance connected with the superior mesenteric vessels, which presented the histological structure of placenta.

I still hold the hypothesis of Schlagenhaufer to be the most satisfactory for his own case and that of Brens; although he may have gone too far in claiming that the intravascular villous growths in the other teratomata which he cites are also derivatives of an anlage of the chorion.

DESCRIPTION OF THE ILLUSTRATIONS.*

ABBREVIATIONS. Bl.V., Blood-vessels; Ca., Maternal capillary; Ep.W., Epithelial wandering cells; Fib., Canalised fibrin layer; L., Langhans' layer; Sy., syncytium; Tr., Trophoblast; U.M., Uterine muscle; V., chorionic villus.

PLATE I.

FIG. 1. Dr. Edgar's tumour. The uterus laid open from before, showing the tumour within it. Owing to the contraction of the muscle when the organ was opened the prominence of the growth is considerably exaggerated. See pp. 33 and 42. X. Muscle is seen to be drawn up into the tumour in the overhanging edge and the mucous membrane near this had the character of young decidua; see fig. 23. About half natural size.

FIG. 2. The same specimen in section. The darkest patches are recent hæmorrhages. The thickness of the uterine wall is much exaggerated, as already explained.

FIG. 3. A section of a placenta about the end of the third month in situ. It shows a villus (V.) with trophoblast still persistent at the tip, free syncytial giant cells in the intervillous space among the maternal blood, canalised fibrin layer (Fib.), decidua serotina, syncytial wandering cells (Ep.W.) in its deeper layers, and the edge of the uterine muscle (U.M.).
Winkel, 14 mm. apochromatic; Oc. 1. × 60.

FIG. 4. The developing placenta about the twelfth day. Showing portions of chorionic villi, which have very large masses of trophoblast at their peripheral ends. The distinctness of the two layers is somewhat impaired by the post-mortem changes. Large masses of the Langhans' layer derivatives occupy most of the field; the syncytial border and syncytial masses here and there are quite distinct. From a preparation given to the author by Prof. Marchand.
Winkel, 14 mm., apo. and Oc. 4. × 150.

FIG. 4a. A villus attached to the decidua; third month. The fibrin layer is defective at this point, and the trophoblast and decidua cells mix to some extent. The distinctness of the trophoblast cells is lost through degenerative changes (or bad fixation), but the large size and deep staining of their nuclei contrasts with the small size relative to the cell bodies and poorness in chromatin of those of the decidua cells.
Winkel, 14 mm. and Oc. 4. × 200.

FIG. 18, on Plate I. A young syncytial cell (intermediate form). Showing two small round bodies in round clear spaces in the cytoplasm near the nuclei, which represent the beginning of vacuolation.
From a drawing by Wenzl. × 640.

* A magnifying glass may be used with advantage.

PLATE II.

FIG. 4b. Ovum of the guinea-pig, 6 days and 12½ hours after the coitus, almost completely imbedded in the uterine mucous membrane. The hole in the uterine epithelium is blocked by the outermost cells of the ovum and somewhat contracted. Its edges are sharply defined from the ovum. The latter is already differentiated into outer and inner sets of cells. Round about it a cavity has formed by complete destruction of a zone of connective tissue, and the degenerative changes can be traced through a still wider zone.

From v. Spee, "Die Implantation des Meerschweincheneies," fig. 11. × about 320 d.

FIG. 5. Chorionic villus, showing very marked hypertrophy of the epithelium, both layers participating. From a case in which curettement was followed by complete cessation of symptoms which had suggested chorionepithelioma. From a preparation given to the author by Prof. Marchand.

Winkel, 14 mm., apo., Oc. 1. × 85.

FIG. 8a. Photograph of the same section as fig. 8 on Plate III., showing part of the villus, which is in a state of hydatidiform degeneration, and the extensive epithelial outgrowth. The figure does not extend far enough to show the uterine muscle, which was somewhat infiltrated by the outermost cells of the epithelial expansion. The position of the preceding figure is outlined. Compare fig. 9a.

Zeiss, aa, 24 mm., no Oc. × 30.

FIG. 9. Portion of a hydatidiform villus with epithelial hypertrophy, from a case of chorionepithelioma. The uterine wall is slightly infiltrated. From a preparation given to the author by Prof. Marchand. (Case Marchand-Gunther: Risel, No. 2, patient æt. 53.)

Winkel, 14 mm., Oc. 1. × 60.

FIG. 9a. Chorionepithelioma with villi or malignant mole. Villi are seen to the left; one of them is almost normal. The invasion of the uterine wall by tumour is seen to the right. From one of the cases of Julius Neumann. Preparation given to the author by Dr. Hitschmann, Vienna.

Zeiss, aa., 24 mm., no Oc. × 24.

PLATE III.

FIG 6. Typical masses of chorion-epithelioma invading the uterine muscle. Case 1. The tumour tissue is distinguished by its darker shade. The remains of uterine muscle among the tumour processes produce a sort of alveolar structure. The dark masses with many nuclei are the syncytium. Here and there detached masses of it are seen, some of which simulate hypertrophied muscle fibres.

From a drawing by Jacob Wenzl, Vienna. × 85.

FIG 8. A small portion of a villus showing the origin of the tumour from the epithelium; the continuity of the various cell formations with one or other layer is obvious. Karyokinetic figures are numerous in the

Langhans' layer cell masses. Compare fig. 8a on Plate II. From Dr. Haultain's case of chorionepithelioma.

From a drawing by Wenzl. × 220.

Fig. 13. A uterine blood-vessel invaded by tumour. The attacking cells have appeared under the endothelium at two points, and large wandering cells of intermediate character have also crept round to the other side of the vessel. The uterine tissues show reactive round-celled infiltration. In the vessel, at a point where the endothelium has already broken down, there is a small thrombus. In the vessel there is a clump of tumour cells. Compare fig. 14 (photograph) on Plate VII.

From a drawing by Wenzl. × 85.

Plate IV.

Fig. 7. Chorionepithelioma tissue from an area in which it formed a regular layer like the floor of an ulcer. Here it happened to consist principally of Langhans' layer cells, with irregular dark masses of syncytium scattered through it. The blood-vessels at the border of the tumour have the walls on the side next it replaced by tumour tissue. The connective tissue is converted into a sort of granulation tissue. There is an outlying mass of tumour (Sy.) amidst it.

From a drawing by Wenzl. × 85.

Fig. 12. The tumour growing into the mouth of a uterine sinus. The vessel is for the most part lined with syncytium; to the left are traces of the endothelium. The uterine tissues are infiltrated with tumour cells of very varied shapes and sizes and number of nuclei; they have themselves to some extent assumed the character of granulation tissue. The resulting confusion of cell forms is difficult to unravel, but less so with the microscope than in the drawing; most of the larger vesicular nuclei indicate tumour elements. To the right and below is a mass of typical tumour. Ca., a capillary with well-preserved endothelium and tumour cells just outside it. From case 2. Compare fig. 13.

From a drawing by Wenzl. × 220.

Plate V.

Fig. 10. Cell mass from case 2, showing the large decidua cell-like elements, and forms intermediate between the Langhans' layer and the syncytium. The mass is surrounded by blood and thrombus. Many of the individual cells contain several nuclei. Compare fig. 20, Plate VI.

From a drawing by Wenzl. × 130.

Fig. 11. Vacuolated syncytium with masses of Langhans' layer elements imbedded in it. To the left is uterine tissue infiltrated with epithelial wandering cells. Compare fig. 12. This and the preceding figures show the large number of leucocytes which are usually found in the neighbourhood of the tumour tissue, and their small size compared with the tumour cells. Case No. 2.

From a drawing by Wenzl. × 130.

FIG. 15. Transverse section of a process of tumour extending along the wall of a blood-vessel. The lumen is filled by the tumour and not much of the wall remains. From case 1.

From a drawing by Wenzl. × 170.

FIG. 16. An isolated mass of syncytium in a blood-vessel of the uterus, attached to the wall and in process of forming a metastatic growth. See p. 49. Case No. 1.

From a drawing by Wenzl. × 240.

FIG. 17. A mass of syncytium, showing the bristle edge (so-called ciliated border) and clear individual cells differentiated (?) within it. See p. 45. A number of deeply-stained threads of fibrin are seen among the ends of the protoplasmic processes and also a number of red corpuscles and leucocytes. The syncytium is attached to lung tissue. Kelly and Teacher case.

From a drawing by Wenzl. × 640.

PLATE VI.

High power photomicrographs to illustrate especially pp. 45 to 47. Zeiss, 3 mm., apo., N.A. 1·40, and 4 proj. Oc. Watson parachromatic condenser.

FIG. 19. Slightly hypertrophied individual cells (Langhans' layer), showing karyokinetic figures and the delicate protoplasmic reticulum.

From Case 1. × 800.

FIG. 20. A similar mass of tumour cells, showing intermediate cell forms; cells with two or three nuclei; two small giant cells with several nuclei, and a large vacuolated mass of syncytium with similar cytoplasmic characters. From Case 2.

Reichert, 8 mm., semi-apo., Zeiss Comp. Oc. 8. × 300.

FIG. 21. Old syncytium showing the alveolar structure of the cytoplasm. This and the adjacent individual cells are drawn out by a hæmorrhage in the neighbourhood. The same mass of syncytium, but in a different section of the series, is seen in fig. 13, Sy. × 600.

FIG. 22. Large wandering cells of Langhans' layer infiltrating uterine tissues. The deeply-stained fibrous matter is remains of connective tissue.

From Case 1. × 600.

FIG. 23. Young decidua cells from case 1, for comparison with the tumour cells. × 600.

PLATE VII.

FIG. 14. Photograph of part of the same vessel, as is shown in fig. 13, Plate III. From a neighbouring section of the series.

Winkel, 14 mm., Oc. 1. × 85.

FIG. 24. Cells from a degenerated and partly necrosed mass of chorion-epithelioma. Kelly and Teacher case.

Reichert, 8 mm., etc. × 300.

FIG. 25. Part of a typical mass of chorionepithelioma, showing the two leading cell forms. From case 1.

Same as above. × 300.

FIG. 26. The chorionepithelioma of teratoma; from a section of the primary tumour in Schmorl's case. It shows a mass of syncytium with individual cells imbedded in it; the embryonic connective tissue surrounding the chorionepitheliomatous tissue and the epithelial layer which at one point is tucked in so as to resemble a gland tubule. The fact that this epithelium presents two layers like the chorionic epithelium is not brought out in the photograph.

Winkel, 14 mm., apo., Oc. 4. × 75.

FIG. 27. Carcinoma syncytiale. A carcinoma of the body of the uterus showing cell forms similar to chorionepithelioma, but a totally different mode of growth. See Part II. From a preparation of Prof. Muir.

Winkel, 14 mm., apo., Oc. 4. × 150.

PLATE I.

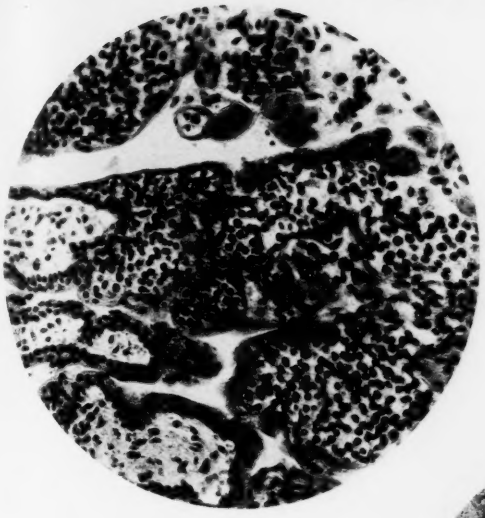


Fig. 4.

Fig. 1.

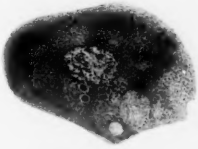


Fig. 18.

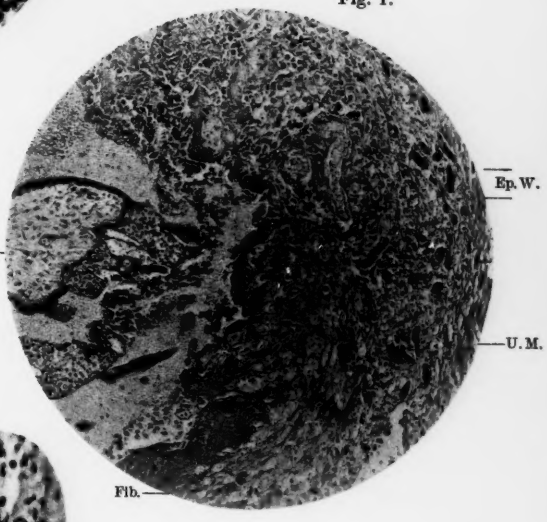


Fig. 3.

Fig. 4a.

Fig. 2

PLATE II.

Fig. 4b.

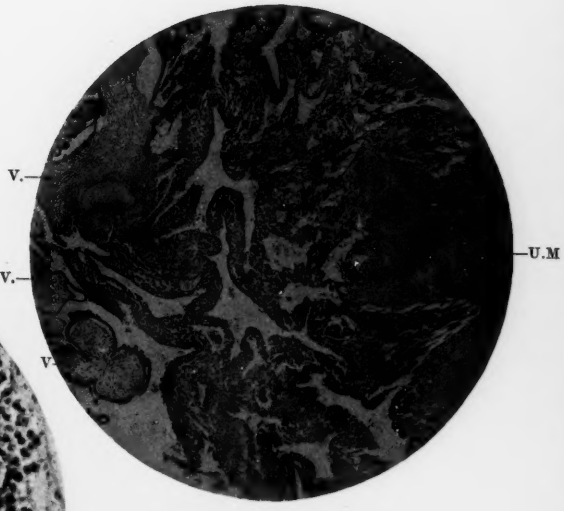


Fig. 9a.

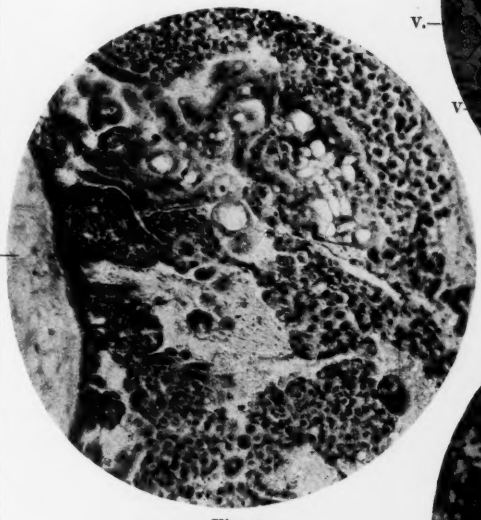


Fig. 5.

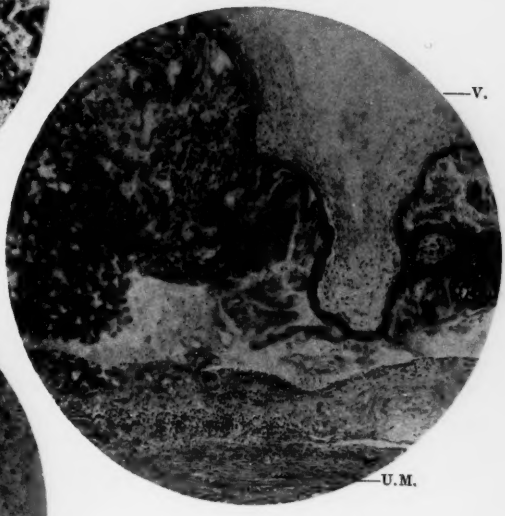
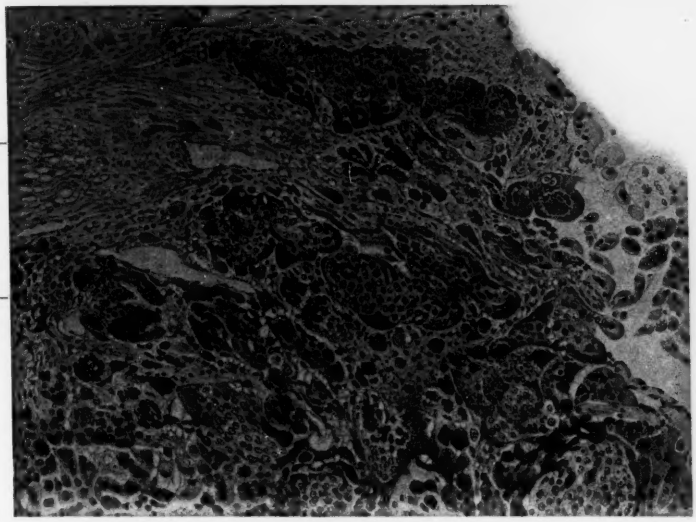
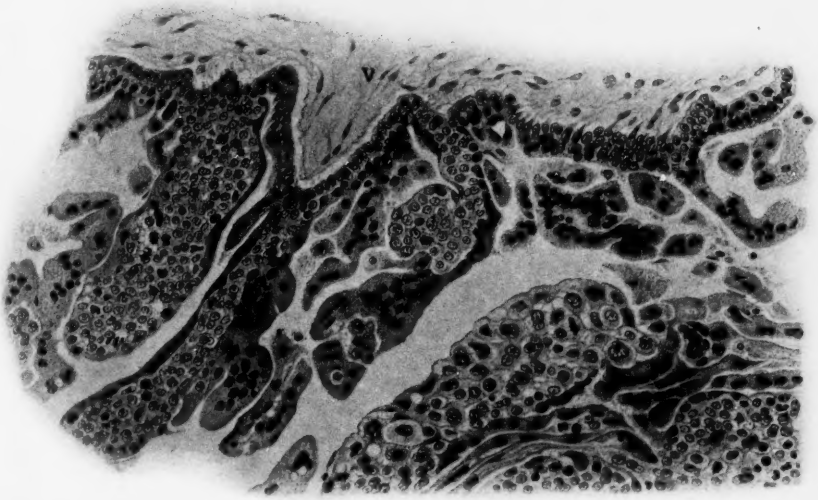


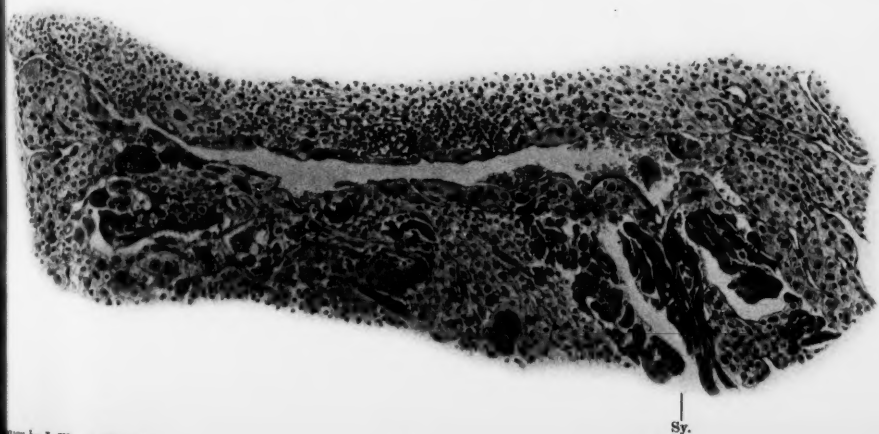
Fig. 9.

Fig. 8a.

PLATE III.







...wn by J. Wenzl, Vienna.

PLATE IV.

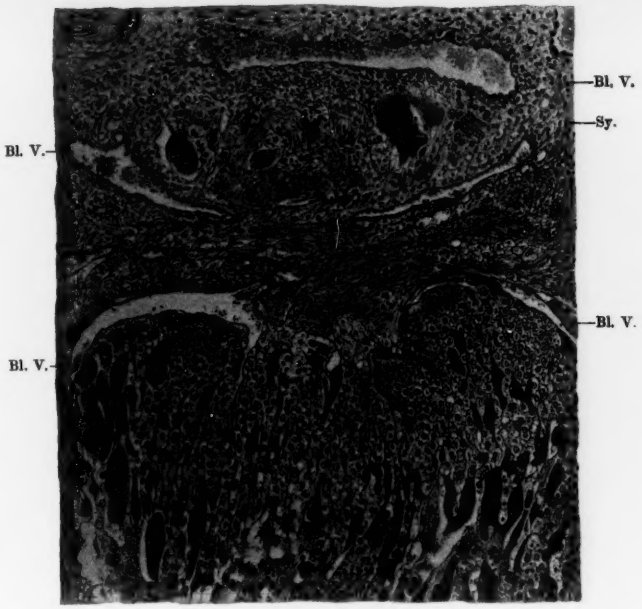


Fig. 7.

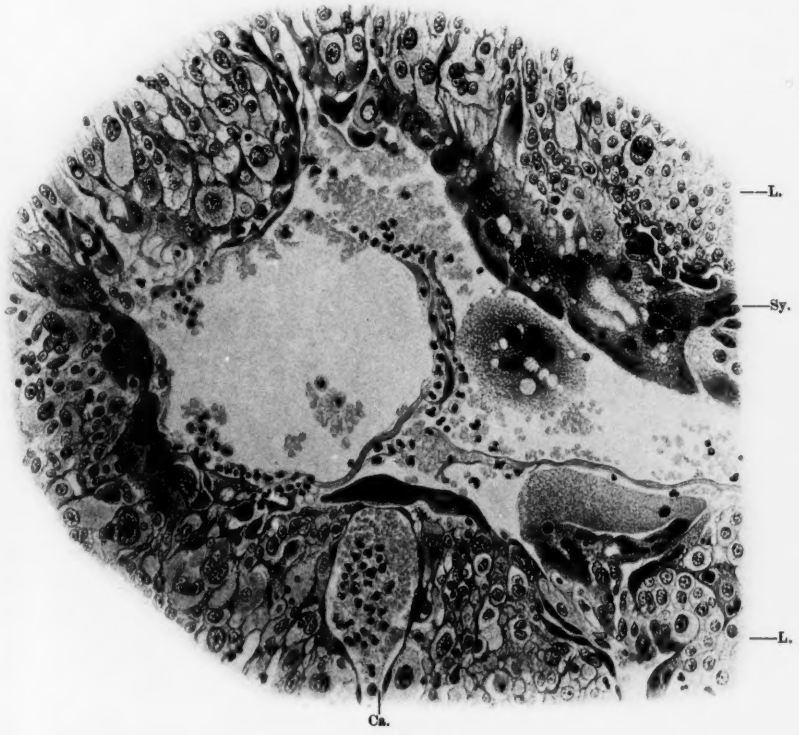


Fig. 12.

Drawn by J. Wenzl, Vienna.

PLATE V.

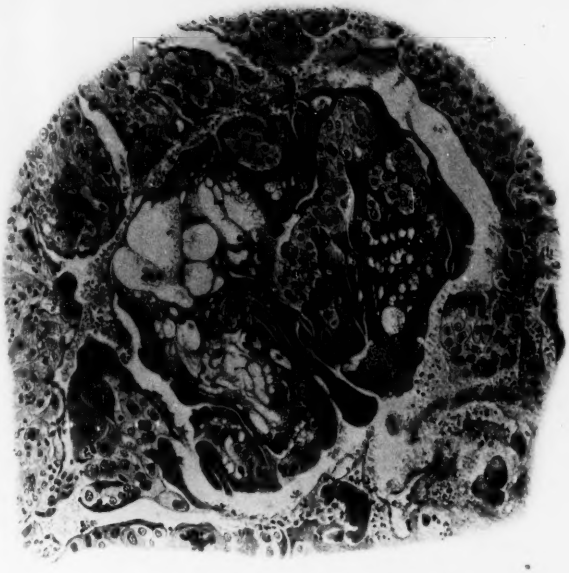


Fig. 11.

Fig. 17.

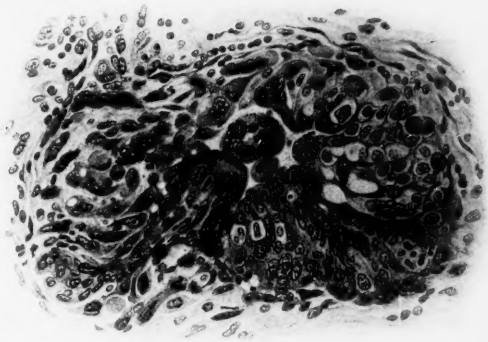


Fig. 15.

Fig. 10.

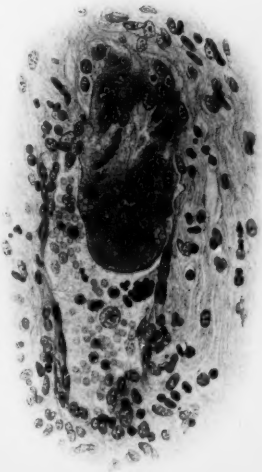


Fig. 16.

Drawn by J. Wenzl, Vienna.

PLATE VI.

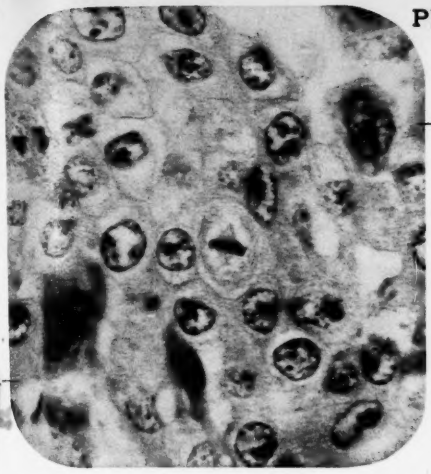


Fig. 19.

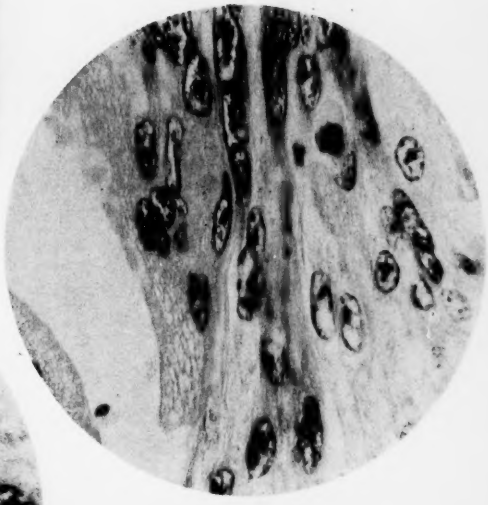


Fig. 21.

Fig. 22.

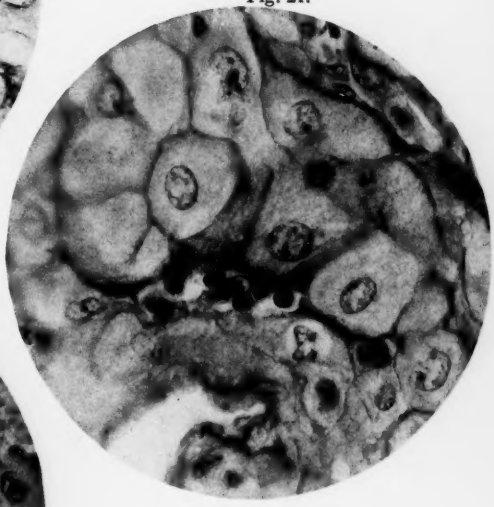


Fig. 23.

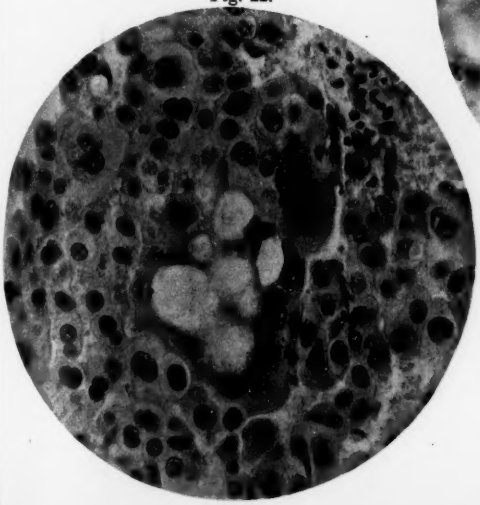


Fig. 20.

PLATE VII.

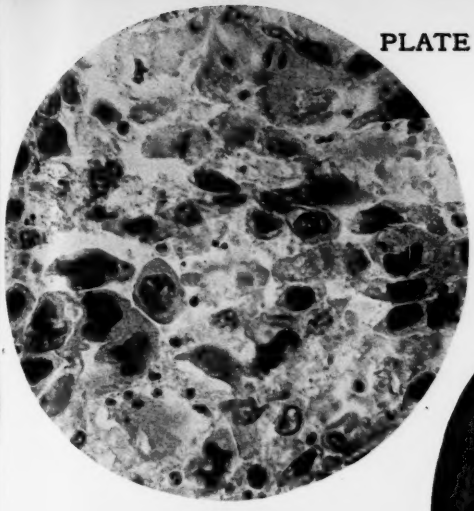


Fig. 24

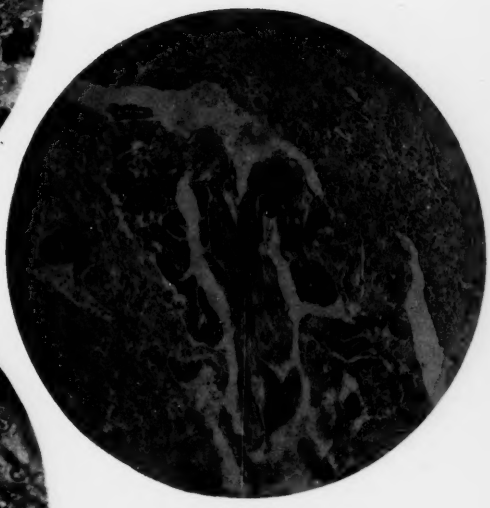


Fig. 14.

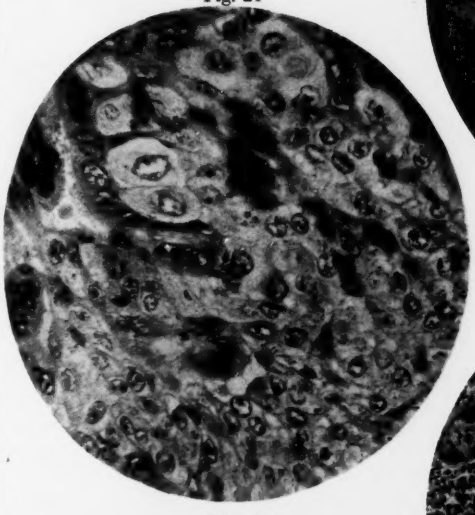


Fig. 25.

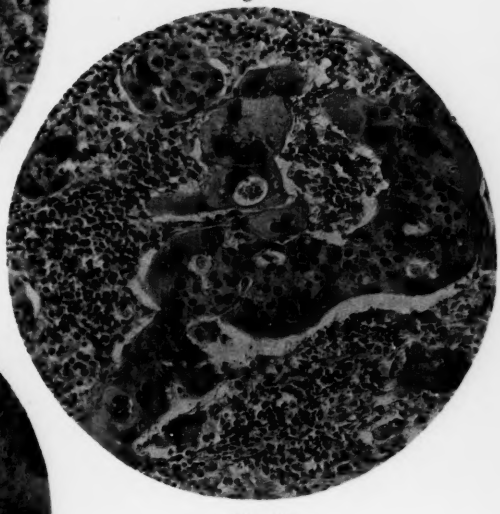


Fig. 27.

Fig. 26.

A CASE OF EMBRYOMA OCCURRING IN THE MEDIASTINUM.*

By JAMES RITCHIE, M.A., M.D., *Reader in Pathology in the University of Oxford.*

(From the Department of Pathology, University of Oxford.)

The following paper is intended to give an account of a case where a dermoid cyst occurred in the anterior mediastinum, and where there was associated with this common tumour a malignant growth of very unusual characters. The specimen has been in the laboratory for some years, but it is only recently that I have been able to arrive at a probable view of its real nature.

A young man, aged 24, was first seen on May 15th, 1900. He complained of pains in the right mammary region, with cough and general feeling of illness of three days' duration. His pulse-rate was 116, his respirations 36 per minute, and his temperature was 101°F. On examining the chest it was noted that the right side seemed to expand less freely than the left; on percussion the note was resonant all over the chest, back and front, except in an area of circular shape extending from the lower margin of the first left rib down to the site of the normal cardiac dullness, and from the right margin of the sternum, opposite the first right intercostal space to a point about two inches to the left of the sternum. On auscultation an area, about two inches in diameter, of fine friction was heard, opposite the site of the right nipple. The breath sounds on the right side were normal, though here and there slight variations in intensity were observable. There were no accompaniments. On the left side, however, the sounds were more feeble all over the lung, and over the area of dullness noted no respiratory murmur could be heard. The cardiac area appeared normal and nothing was to be noted with regard to the heart sounds. There was no evidence of disease elsewhere in the body. On making strict enquiries among the patient's friends it was found that the illness had had a longer duration than that stated by the patient himself. He had been observed to be out of health and not so active as formerly for about three months, and for about six weeks previously had every morning spat up a quantity of bright-red blood. Taking all the circumstances into account the diagnosis arrived at was that a malignant tumour existed in the mediastinum pressing especially on the root of the left lung, and

* Demonstrated to the Obstetrical Society of London on June 3rd, 1903.

that a secondary growth or secondary growths were present in the right lung, which last accounted for the attack of pleurisy. The following is the subsequent history of the case. The pain and the friction over the right lung abated, the temperature fell to nearly normal, and the pulse to about 90. Certain symptoms, however, remained. Constant and very distressing cough was present. Although the pulse-rate was diminished there was no corresponding fall in the rate of breathing, and from time to time there was a return of the hæmoptysis. About a week after the patient was first seen, dyspnœa became a very acute symptom. The breathing was very rapid and laboured, without there being any evidence of actual mechanical obstruction to air entrance or exit. The patient became, during the next five days, gradually weaker and died apparently from exhaustion.

A *post-mortem* examination was held on the following day. The body was fairly well nourished; on opening the thorax a small quantity of free fluid was found in both pleural cavities, and there were some very recent adhesions over the front of the right lung. A mass of new growth was observed occupying the anterior mediastinum, projecting over the root of the left lung and extending downwards in front of the pericardial sac. The whole of the contents of the thorax were therefore removed *en masse* (Fig. 1). It was found on palpation that the tumour apparently consisted of two parts; towards the left and inferiorly was a cyst, and above and to the right there was attached to it a solid mass. The following measurements were taken after the specimen had been preserved in formalin. Length of mass from above down 15 cm., breadth across centre 12 cm., thickness from 5 to 6 cm. The cyst measured 7 cm. from above down. On opening the latter its dermoid nature was evident from the facts that it was filled with sebaceous matter and from the walls projected many fine hairs. Its cavity was very irregular and in its greatest extent it measured 5 cm. from back to front. On incising the solid part of the growth this was found to be continuous with the wall of the cystic part. Its main naked eye character was the presence of great areas of hæmorrhage and its substance could be very easily broken down. Both lungs were riddled with small circular tumours varying in size from small specks just visible to the naked eye up to about 5 cm. in diameter. These secondary growths had the same general naked eye appearances as the solid part of the primary tumour and likewise contained a great number of hæmorrhages. There were several similar tumours in the liver and one about 2 cm. in diameter in the spleen. Except that the lungs

were œdematous and congested, especially round the tumours, they and the other organs of the body were normal.

Pieces of the tumour were fixed in perchloride of mercury, hardened in alcohol, embedded in paraffin, cut and stained, mostly in hæmatoxylin, eosin and aurantia. From such specimens the following facts were elicited:—The dermoid part of the tumour was lined by a very elementary badly staining epithelium, consisting of a few layers of cells resembling the more superficial cells of the normal *rete malpighi*. Sometimes there was an attempt at a papilliform arrangement, but usually the surface was fairly smooth and broken here and there by the occurrence of crypts corresponding to the openings of sebaceous glands. To the naked eye this gave to the surface a coarsely granular appearance. These crypts were lined towards their mouths with rudimentary epithelium and below contained cells resembling the ordinary cells of sebaceous glands. These sebaceous glands were, however, much simpler in structure than normal and appeared to consist of a simple flask-shaped structure without convolutions. At one side of a crypt there was frequently seen a formation which manifestly represented a hair. These hairs were very thin and badly formed. Beneath the epithelium and surrounding the glands and hair follicles was an imperfect connective tissue of a myxomatous nature. This contained many fibres of non-striped muscle and close to the surface a rich supply of capillaries. Deeper down there was an abundant formation of fat cells with bundles of connective tissue running between them. Sections made through that part of the cyst wall which became incorporated with the solid tumour showed the presence either of subsidiary cysts or of diverticula of the main cyst cut transversely. The epithelium here (Fig. 2) also was very elementary, but had more tendency to be arranged in somewhat complicated papillæ covered by cornified cells having little adhesibility. Here also there were elementary hairs and sebaceous glands and also capillaries and these structures abutted directly and were to some extent intermingled with the parts of the tumour to be next described. The greater portion of the solid part of the tumour consisted of very irregularly shaped areas of badly staining material which evidently was made up of necrosed cells of various shapes and sizes. In these the outlines of the protoplasm could often be made out, and also the remains of the nuclei which frequently had a broken up appearance. There was also evidence of large hæmorrhages having taken place in connection especially with these areas, there being numerous red blood corpuscles, partly apparently normal, often showing evidences of break-

ing down, and where they abounded there were many large phagocytic cells containing their remains. Interspersed very regularly among the necrosed areas were smaller masses of cells showing good staining reactions. These cells were very varied in character, shape, and size. (1) The simplest were loosely arranged with reference to one another (Fig. 6), often not lying in contact, and possessed a round or oval nucleus staining intensely, and also protoplasm varying in amount and staining slightly of a uniform pink tint. Some of these cells were circular and 8-16 μ in diameter. Others were oval and were from 32—48 μ long and from 24—30 μ broad. Interspersed irregularly among these were large protoplasmic masses of irregular shape and often possessing processes of different lengths. The protoplasmic body might here measure up to 120 μ in diameter and often contained an irregular oval nucleus with the chromatin network more open than in the case of the smaller cells. These cells seemed sometimes to be having a phagocytic action on the smaller cells. Sometimes the nucleus could be seen to be undergoing karyokinesis and sometimes it was irregularly lobate. Among these cells were numerous red blood cells. (2) At other parts the tumour showed masses of closely packed polyhedral cells 12—30 μ in diameter (Fig. 5) with faintly staining protoplasm containing a few fine granules and showing great tendency to vacuolation. The nuclei were usually oval, 8—12 μ in longest diameter, often showing one or two nucleoli. They were very poor in chromatin and often vacuolated; in some cases mitosis was observed to be taking place. These closely packed masses of cells presented somewhat of an alveolar arrangement being cut up into smaller masses by bands of elliptical cells containing oval deeply staining nuclei. These septa often contained blood spaces lined by similar cells. Abutting on these blood spaces there were frequently noticed large irregular branching masses of protoplasm less in size, but similar in appearance to the protoplasmic masses next to be described. Glycogen could not be demonstrated in the polyhedral cells, but the material used for this purpose had been preserved many months in formalin. (3) A striking feature of the tumour was the occurrence of blood sinuses. These occurred very irregularly, sometimes in the midst of the cell masses last described, sometimes separated by only a few layers of the polyhedral cells from the necrotic areas. They varied in diameter from a few μ, as in the case of those just alluded to as seen in the septa of the cell masses, up to large irregularly shaped spaces measuring up to 300 μ in diameter. These sinuses were lined sometimes in whole, sometimes in part, by flattened endothelial-like cells. Occasionally they appeared

to abut directly on the polyhedral cells. But often in connection with the sinuses were seen the most notable cells occurring in the tumour. These were large sheets of protoplasm of very irregular shape (Figs. 3 and 4), being bent round the irregular outlines of the sinuses and often throwing projecting knobs into the latter. These masses varied in size from a few μ up to masses 500 μ in length. The protoplasm in these structures stained intensely with eosin and had a finely granular appearance. It contained usually a large number of very irregularly disposed nuclei which might reach 50 μ in diameter. These often contained nucleoli from which strands of chromatin ran to the nuclear membrane and between these strands were irregular vacuoles. From the protoplasmic masses prolongations ran among the surrounding cells and often among the latter could be seen cells having the same staining reactions and which were apparently not connected with blood sinuses. Cells intermediate between the large masses and the elliptical cells often lining the sinuses could be observed and also between the large masses and the cells described under heading (1). Some of these cells were quite small,—about 12 μ in diameter, and the protoplasm was stellate. Especially in the parts of the masses which projected into the blood sinuses there were often large vacuoles. The sinuses contained apparently normal blood in which, however, could be seen detached tumour cells. The number of sinuses present varied much in different parts of the growth—large areas being observed which appeared entirely free from sinuses. In many places the necrotic areas had in them infiltrations of leucocytes. The secondary growths of the tumour had the same general characters as the solid part of the mediastinal mass.

To sum up the features of the whole tumour one may say that in the mediastinum of this young man there existed a dermoid cyst; that attached to and forming part of the wall of this cyst was a solid growth of a malignant nature; that this malignant part was composed largely of dead tissue, but contained areas of living cells; that these cells were of three main types, (*a*) closely packed polyhedral cells (Fig. 5), with both nucleus and cytoplasm much vacuolated, (*b*) enormous protoplasmic sheets (Figs. 3 and 4), multi-nucleate and with intensely staining cytoplasm, which sheets were largest when bounding blood sinuses, (*c*) small cells (Fig. 6) not in such large numbers as the other two types whose staining reactions conformed closely with those of the second group of cells but which were frequently mono-nucleate.

In looking at this tumour the most characteristic feature always

appeared to me to be the sinus formation and the presence of the great sheets of protoplasm, and the only theory which I could form of the nature of the growth was that it belonged to the group of angio-sarcomata. I thought it possible that the formation of such protoplasmic masses might be supposed to find a homologue in normal tissues in the method in which new capillaries are formed in the fœtus and in granulation tissue. The passage of a protoplasmic process from an endothelial capillary cell into the surrounding tissue, the hollowing out of the aspect of the cell directed towards the capillary lumen, the multiplication of the nucleus and the stage when the wall of the diverticulum may be formed of such a multinucleate cell before its division into a definite endothelium—all these stages are familiar. What from the present point of view is important is that in slowly formed or unhealthy granulation tissue such, for instance, as may occur in the line of demarcation in a gangrenous limb, the process of division of the cells may be apparently delayed and multinucleate cells of very considerable size may be found in capillary walls marking the spot where an attempt at a new budding has been made. A difficulty in such a view was found when the other cells of the growth were considered, but the mode of formation of the cells outside the limiting cells of the blood-spaces in ordinary angio-sarcomata is also often not quite clear. Such a relationship of the tumours similar to that just described has been suggested by Malassez and Monod. My attention was first called by Mr. Richard Muir, of the Department of Pathology in the University of Edinburgh, to the similarity which the mediastinal growth bore to the structure of the tumours formerly called by the name of deciduoma malignum which are now more frequently denominated chorion-epitheliomata—the tumours which have been observed developing in the uterine wall after parturition and which usually present a high degree of malignancy. Since this suggestion was made to me I have had the opportunity of examining a considerable number of sections of such tumours, and I have no hesitation in saying that the solid part and the secondary tumours of this mediastinal growth are histologically identical in structure with these chorion-epitheliomata. The large protoplasmic masses correspond to the syncytial cells derived in the chorion-epithelioma from the similar cells covering the chorionic villi, the polyhedral cells correspond with similar cells in the uterine tumours which are supposed to come from the Langhans' layer of the villi and the intermediate cells described above are also found in the other growths. This mediastinal tumour must, therefore, be ranked among the tumours which are identical with the chorion-

epitheliomata and which have been described as occurring in parts of the body other than the uterus after parturition, *e.g.*, in the testicle, the reproductive organs of non-parturient females, etc. Another similar tumour has been described by Schlagenhaufer, who, in a growth in the testicle with secondary growths in the lung, found the main mass to resemble a chorion-epithelioma, while there were also pieces of squamous epithelium, spaces lined by cylindrical epithelium, and some tissue resembling fœtal lung. The tumour I have described must, therefore, be looked on as one of very great interest. Malignant tumours associated with dermoids are by no means rare. In certain cases these have been simply of a carcinomatous or epitheliomatous character and have plainly been derived from the epithelial structures which form the main part of most dermoids. A number of cases of a different kind have been collected by Jores, and also by Montgomery. In most of these the primary tumour has contained, besides epiblastic structures, elements derived from the mesoblast, such as cartilage, etc., and also often hypoblastic structures, and besides has shown tissues which have usually been described as sarcomatous—the type being that of the round-celled or spindle-celled sarcoma. The secondary growths of these tumours have usually been chiefly sarcomatous, but sometimes carcinomatous elements have been also seen. A case which recently came under my observation probably belonged to this group. In it there was a dermoid cyst of the ovary to which was attached a solid tumour containing chiefly sarcomatous tissue of a roughly round-celled type and also cartilage, non-striped muscle fibre, spaces lined by columnar epithelium, myxomatous tissue and blood spaces lined by flat endothelial cells, but showing nothing like a syncytial formation. The patient from whom it was removed suffered from a local recurrence within a few weeks of the first operation and died very shortly thereafter. No post-mortem was obtained. Such malignant dermoids have usually been observed in connection with the ovary. In the mediastinum a number of dermoids have been recorded by Ekehorn and these have chiefly been simple cysts, though the fact is often noted that they contained such mesoblastic structures as bone. The last occurrence has been denied by Wilms, who states that mesoblastic structures are only found in dermoids of the ovary or testicle, where an origin from embryonic cells is possible, his view being that the mediastinal dermoids are in every case merely epiblastic inclusions. A review of the descriptions of dermoid tumours suggests that cases like that described by Schlagenhaufer and such as I have described above are extremely

rare. The syncytial masses are very striking objects in the microscopic preparations and they could not have failed to have been observed even if their significance had not been realised.

When we come to consider the probable pathology of the tumour two views are possible. Either there was a dermoid caused by an inclusion of the epiblast of the third visceral cleft in connection with which the thymus gland is developed, and along with this a sarcoma of a special kind happened to be formed, or, this tumour is really a teratoma formed from an ovum included in the thorax or from an abberant division of the cells of the ovum from which the individual in whose body it was found was formed. The inclusion theory would be the most probable, for it is almost necessary to suppose that part of the trophoblast of an ovum was present and that from this a growth having all the characters of a chorion-epithelioma was developed. With reference to the view that the growth might really consist of two tumours,—a dermoid with an accidentally associated sarcoma, the characters of the latter at once claim attention. Though at first I was inclined to look on it as a angio-sarcoma, I have never seen nor seen described such an angio-sarcoma. The sarcomatous theory of the origin of ordinary chorion-epitheliomata has also been put forward, but here again the extraordinarily special nature of the structure of these is generally most striking and if one compares this structure with the cellular constitution of the placenta one cannot fail to be struck with the fact that their special cellular features are the cellular features of that organ. If we look at the question from the point of view of probabilities we are brought face to face with the fact that in chorion-epithelioma we have a very unusual tumour whose structure resembles a structure which may be normally present in the vicinity and the origin of the tumour from that structure is suggested on as good grounds as the origin of a malignant adenoma from the follicles of, say, the sigmoid flexure. And when as in Schlagenhaufer's case and mine there is in each case a structure which is very probably an included ovum and in each case a tumour which elsewhere has only been observed in situations where it is probably derived from trophoblastic structures there is considerable reason for the opinion that the trophoblast of the included ovum has undergone development along the same peculiar lines as the trophoblast in a case of chorion-epithelioma. Its quiescence for 24 years might well be adduced as a point in favour of Cohnheim's inclusion theory of tumour formation.

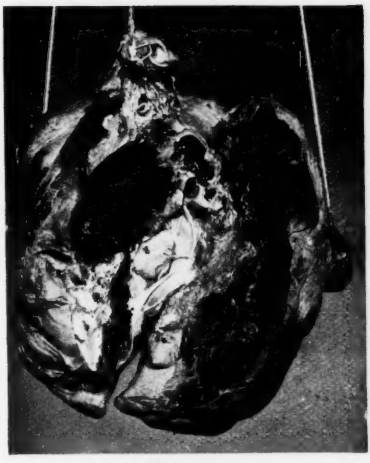


Fig. 1.

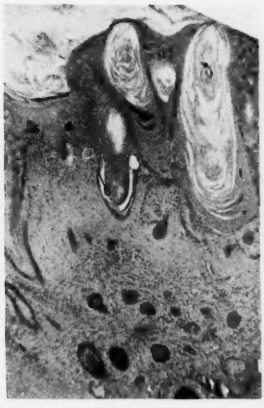


Fig. 2.

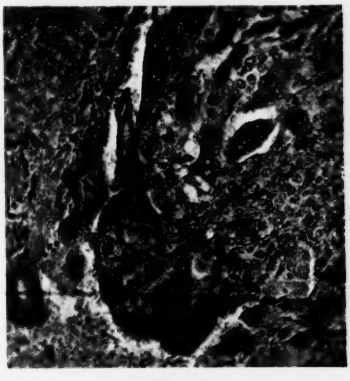


Fig. 3.

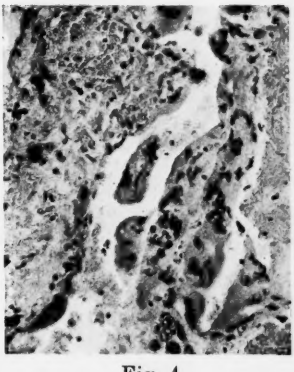


Fig. 4.

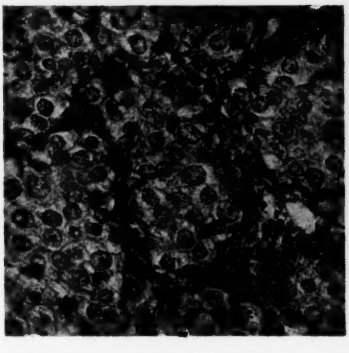


Fig. 5.

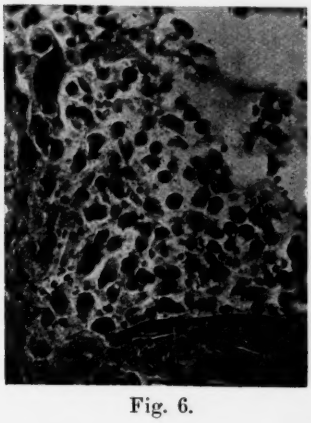


Fig. 6.

References.

Malassez and Monod, *Arch. de Physiologie*, 1878.
Schlagenhaufer, *Wien. klin. Wochenschr.*, 1902, Nos. 22, 23.
Jores, *Virchow Archiv.*, 133, 66.
Montgomery, *Journ. Exp. Med.*, iii., 259.
Ekehorn, *Langenbeck's Arch. f. klin. Chirurgie*, 56, 107.
Wilms, in Martin's *Die Krankheiten der weiblichen Adnexorgane*, ii., 576.

Description of Figures.

Fig. 1. Naked eye view of thoracic contents from left. The left lung and the tumour are chiefly seen. Slices have been taken off the anterior edge of the former and the left edge of the latter. In the lung several circular secondary growths are seen. In the section of the tumour there is above the solid part of the tumour with the hæmorrhagic appearance; below is the dermoid cyst containing the white sebaceous matter. Below the tumour is the apex of the heart.

Fig. 2. Section through the wall of the dermoid cyst, showing flat epithelium, elementary hair follicles, etc.

Fig. 3 and 4. Blood sinuses, showing the syncytial cells in the walls. In fig. 3 these cells abut by their other aspects on the polyhedral cells; in fig. 4 the cells rather abut on necrotic areas.

Fig 5. The areas of polyhedral cells with roughly alveolar arrangement.

Fig. 6. The cells described under heading (1)—chiefly mono-nuclear and having the staining reactions of the syncytia.

ON MALIGNANT CHORIONEPITHELIOMA.

By F. MARCHAND, *Professor of Pathology in the University of Leipsic.*

(Translated from the German by T. W. EDEN, M.D.)

ALTHOUGH I have already often taken up the pen upon this subject, and have scarcely anything new to advance, yet I gladly comply with the request of the Editorial Committee of this esteemed journal to furnish a short communication upon the discussion of chorionepithelioma.

I cannot do more, in this place, than offer a brief exposition of our present views upon this remarkable new growth, which has not only awakened great interest among gynæcologists, but also possesses great theoretical importance in regard to theories of tumour formation in general. For we have here to deal with the fact that an embryonic tissue, the product of a new sexual generation, disseminates itself in the maternal organism and not infrequently destroys it. And, further, we find histological characteristics which are capable of throwing light upon other epithelial new growths. Thus we meet with the occurrence and dissemination of cell-forms of undoubted ectodermal origin, entirely resembling mesodermal cells, a peculiarity which was not understood until it was found that an entirely analogous dissemination of ectodermal cells of the developing ovum was found in the decidua in normal pregnancy, and even more in certain cases of vesicular (hydatidiform) degeneration.

It is comprehensible that authors who first recognised tumours of this nature as something unusual, above all Sänger and Pfeiffer (Chiari), should have designated them as "decidual sarcoma" (deciduoma). I may remark, historically, that to Gottschalk belongs the credit of having first rightly interpreted the masses of the so-called syncytium of the chorionic villi in a malignant tumour of this kind with metastases, but he erroneously regarded a part of the tumour as sarcoma arising from the stroma of the villi. Then L. Fraenkel, in a case described by him as carcinoma of the uterus, regarded the growth of the epithelial syncytium as the essential element, without, however, recognising the nature of the other elements of the tumour, which he regarded as quite different from the so-called "deciduoma" of Sänger. Upon my own observations the latter work had no influence, because they were completed on its appearance. By a specially fortunate circumstance it chanced that I

was able, in a case of hydatidiform mole in the uterus, to recognise the same epithelial formations as in the two layers of the chorionic mantle, and the invasion of the muscular wall of the uterus by these cells, as in malignant chorionepithelioma.

A difficulty presented itself in forming an opinion upon the origin of the tissue forms present in this growth, viz., the very diverse opinions which existed upon the two layers of the chorionic epithelium, the well-known multinucleated protoplasmic covering of the placental villi (which later was named "syncytium"), and the more recently discovered "cellular layer" of Langhans. While several embryologists (*e.g.*, Kastschenko) held both layers to be fœtal, others having in view the conditions found in animals, referred the outer layer to a maternal, the inner layer to a fœtal origin. Inasmuch as at that time I had not had the opportunity to decide this question by personal study of early human ova, I had to assent to one of these views, and I felt obliged to decide upon the latter, although I had already, both in regard to tumour formation and vesicular mole, frequently pointed out that it was often impossible to make a distinction between cells arising from the superficial layer and those arising from the deep layer. I regard as of the greatest importance, the observation that the malignant growth actually arises from the entire epithelial covering of the villi, that at least a part of the new growth, both in the primary tumour and in the metastases is of fœtal ectodermal origin, a view which later was to be strenuously opposed by a number of authorities.

It is clear that conditions found in animals cannot be directly employed in settling this question owing to the great differences between the human placenta and that of lower animals. Opinion upon single points still oscillates to and fro. In the rabbit, where the formation of abundant syncytium from the uterine epithelium can easily be made out, some embryologists refer the entire syncytium of the placenta to this source, but I have myself brought forward the observation that before the implantation of the ovum in the uterus, an undoubted syncytium or plasmodium is formed from the fœtal ectoblast.[1] And, further, it appears that these two different syncytia intermingle in parts so closely with one another, that it is often practically impossible to distinguish the one kind from the other. Why should it not be the same in the human chorion, and thus in the tumour formation both maternal and fœtal elements may participate? But inasmuch as other observations have, in my opinion, conclusively proved that the syncytial layer of the chorionic

mantle of the human ovum is of fœtal origin, this question must also be regarded as definitely settled for the tumour also.[2]

A second difficulty frequently met with consists in the fact that the new growth itself may present such different appearances that it is often truly difficult to refer it to one and the same source. While in one series of cases the same arrangement of the tumour tissues occurs as in the epithelial tissues of the young human placenta (cell-buds, cell columns), yet we find in others (the so-called "atypical" cases) almost isolated cells which spread themselves in the tissues after the manner of a sarcoma, so that they have been taken in part for decidual cells, in part for endothelial cells of the vessels, in part for muscular elements. I proved, however, that these same cells, which, in the cases referred to, were isolated, in other cases were found associated with large syncytial masses and collections of clear cells rich in glycogen. It is not right to regard these isolated elements as "syncytial cells" because their origin exclusively from the syncytium cannot be affirmed.

It has now been demonstrated in so large a number of cases that these apparently widely different epithelial formations arise from the epithelium of villi retained in the uterine vessels, that it cannot be necessary to multiply these cases. The fact that the majority of cases of malignant chorionepithelioma follow the abortion of a vesicular mole, is readily explained if we recollect that this anomaly of the ovum is characterised by the appearanc in it of abundant proliferation of the epithelium of the villi.

In many cases, though by no means in all, chorionic epithelial elements invade the decidua serotina to an unusual extent, destroy the decidual tissues, and even penetrate into the musculature. A similar process is, however, normal in the first stages of pregnancy.

And, further, there exists a series of cases of vesicular mole characterised by such progressive growth of the chorionic villi, that they have been designated "destructive (*destruirende*) vesicular moles." Following Virchow's view that vesicular mole is a kind of myxomatous degeneration of the villi, we could regard this as a variety of "malignant myxoma." This has, however, been shown to be incorrect. We now know that the development of normal villi is initiated by epithelial proliferation, and a similar relation is to be assumed here (in destructive vesicular mole). The formation of the non-vascular stroma of the villi follows that of the epithelium; the former does not grow irregularly into the tissue as in a malignant myxoma, the villi retain their typical shape, as in ordinary vesicular mole, while the epithelium penetrates into the surrounding

tissues in quite irregular fashion. It is obvious that in such cases remains of villi may become deported by the blood stream, and may preserve, to a certain extent, their proliferative activity.

While in most cases the primary localisation of the tumour is found to be in the uterus, there is yet a large series of cases in which the primary growth has not been found at all, so that we might speak of "formation of metastases without a primary growth." These cases also are readily understood when we remember that portions of villi with the chorionic epithelium deported after labour through the circulation, retain their proliferative activity and provoke malignant epithelial growths in the parts to which they have been carried, *e.g.*, the vagina, the lungs, the brain, etc.

It is natural that such tumours should have been regarded as primary sarcomata of the organs in which they were found, before there true histogenesis was understood. Very noteworthy is the fact that in some of these cases the uterine mucous membrane still possessed throughout the characters of the decidua of pregnancy (with regenerated glands), although a long time had elapsed since the labour. By some authorities the formation of the decidua in such cases was explained by the presence in the body of fœtal ectodermal elements, by others it was attributed to the continued presence of a corpus luteum.

The question whether, in those cases in which a malignant tumour is found following an abortion or a vesicular mole, a *primary malignancy* of the chorionic epithelium is to be assumed, must, I believe, be answered in the negative, but it cannot be denied that the proliferative activity of the epithelium and with it, the risk of a malignant growth varies greatly in individual cases. It is difficult to determine wherein this variability consists. Many observations, however, indicate that the increased proliferation depends upon a primary degenerative change in the ovum, and is not in the first place produced by the uterus. The remarkable fact that in many cases of vesicular mole and chorionepithelioma, cystic degeneration of the ovaries was also present, supports this view.

Although the specificity of the tumour can no longer be doubted, yet the possibility cannot, of course, be entirely excluded, that occasionally similar tissue elements may occur in other tumours. Yet, if the *typical arrangement* of the tumour tissues were preserved, any other origin than that from fœtal ectoderm would be very improbable. The question has advanced another step through observations upon tumours of the testis whose histological characteristics in part correspond with those of chorionepithelioma. Such a case

as this the late Prof. Kanthack had apparently seen, and it was in part responsible for his very decisive verdict upon the theory, at that time only recently advanced, of the specific nature of chorionepithelioma. Similar tumours, on account of the large blood spaces in the multinucleated masses, had in France been described as " angioplastic sarcoma." To Schlagenhaufer belongs the observation that tissues which completely resembled those of chorionepithelioma occurred in a testicular tumour which was proved to be a teratoma. Several similar observations were made almost at the same time by Wlassov, Schmorl, and Steinhaus. Two cases have been more recently communicated from my Pathological Institute by Dr. Risel.[3]

In these cases it is apparent that the tissue elements resembling chorionepitheloma stand in immediate continuity with epithelial tubules, so that their epithelial origin cannot be doubted, thus contradicting the view of Kanthack. Since these tumours are teratomata, the embryonic origin of the tissues resembling chorionepithelioma is undoubted, with only this difference, that we have not here to do with embryonic tissue of a younger generation as in chorionepithelioma. Schlagenhaufer has formed the opinion that the tissue arises from a true chorionic epithelium, *i.e.*, from fœtal membranes in the teratoma; he has even gone further, for he believes that the structures closely resembling chorionic villi, observed in a few cases, to have penerated the vessels, are products of the chorionic mesoderm of the teratoma.

This view appears to me to be unproved, for the reason that the structures resembling chorionepithelioma at times form only small islets of tissue, which stand among, and in intimate connection with other forms of tissue, and in the metastases they may occur quite alone. It is readily conceivable that the ectoderm of a teratoma, no matter what view of the origin of the latter we may take, may possess the power to produce tissues similar to the ectoderm of a normal ovum, without necessarily involving the formation of true fœtal membranes. Neither can I share the view of Schlagenhaufer that the growths resembling villi in certain cases of testicular teratoma, represent a true formation of vesicular mole.

I regard them rather as outgrowths from the myxomatous embryonic connective tissue of the teratoma, which, through external conditions (shape of the vessels), have assumed their characteristic form; this, we know, occurs in other tumours, especially myxosarcomata, which have nothing to do with teratomata. In any case this observation supports, if such support were needed, the view

of the similar ectodermal origin of the multinucleated syncytial masses, and the discrete clear cells.

The very remarkable observation by Pick of the occurrence of growths completely resembling hydatidiform villi in a cavity of a dermoid ovarian cyst appears strongly to support the theory of a mole formation from teratomatous fœtal membranes; but it is not quite conclusive owing to the simultaneous presence of an ectopic abortion in the Fallopian tube of the same side.

From the diagnostic standpoint it is an important question whether a "malignant growth" of progressive character should not be assumed in all cases in which after abortion or a hydatidiform mole, remains of villi and active chorionic epithelium remain in the vessels and tissues of the uterus. I cannot affirm that this is so. In my opinion, there is no such thing as "absolute malignancy," and no absolute histological indication of "malignancy." There are undoubted cases in which complete recovery has occurred after thorough curetting of the uterine musculature, even when already much infiltrated with chorionic epithelial cells, and also after extirpation of vaginal metastases. But in other cases, after prompt extirpation of the uterus, rapid dissemination of the growth throughout the body has resulted. We must, in addition to the histological characters, consider the clinical relationships. A sound organism is able, to a certain extent, to combat the further development of proliferative heterogeneous elements. It is not to be denied that in consequence of this circumstance, great difficulties may arise for the gynæcologist in deciding what to do in individual cases. On the one hand he may fall into the error of removing the uterus without sufficient reason, and on the other he may, by postponing operation too long, endanger in the highest degree the life of his patient.

REFERENCES.

[1] MARCHAND. "Placenta des Kannichens," *Schriften der Gesellsch. der ges. Naturwissenchaften zu Marbury.* Bd. xiii., 3, 1898.

[2] PETERS. *Einbettung des menschlichen Eies.* Wien, 1899.
MARCHAND. (1) *Zeits. fur Geburts. und Gynäk.*, 1898. Bd. xxxix. (2) *Beobachtungen an jungen menschlichen Eier. Anatomischen hefte von Merkel und Bonnet.* H. 47, 1902.

[3] W. RISEL. *Ueber das maligne Chorionepithelioma und die analogen Wucherungen in Teratomen.* Leipsig, 1903.

TWO CASES OF "DECIDUOMA MALIGNUM."

By FREDERICK J. McCANN, M.D. (Edin.), F.R.C.S. (Eng.), M.R.C.P. (Lond.), *Physician to In-patients, Samaritan Hospital for Women, London.*

CASE 1. Patient alive and well two years after removal of the uterus by vaginal hysterectomy.

CASE 2. Patient died in hospital—secondary deposits in lungs and vagina.

CASE 1. A woman, aged 35 years, was sent to me at the Samaritan Hospital on July 13, 1901, by my friend Dr. Willan, of Dorking. She was very anæmic and had other signs of excessive blood loss.

History. Since April 1st, 1901, she had been losing blood daily from the vagina. It was supposed that she had had a miscarriage, but the history of the passage of ovuline structures was not definite. The amount of blood lost, which had increased three weeks before admission, had subsequently diminished. She had had four children, the youngest being aged three years. In August, 1900, she had a *miscarriage* at the second month, followed three weeks later by an attack of hæmorrhage lasting fourteen days. Her menstruation then became regular and continued so until April, 1901. She stated that she was getting thinner.

Bi-manual examination. The uterus was felt to be enlarged to the size of a three months' pregnancy, regular in outline, freely movable, and soft in consistence. I decided to operate on July 17th, 1901. The uterus was first dilated and examined with the finger. A distinct swelling was felt at the upper and back part of the uterine cavity. The mucous membrane covering it felt smooth and velvety. On attempting to separate this swelling at its lower part the finger could be introduced into the uterine wall, and the surrounding tissue made me suspicious that I had to deal with a malignant growth. The uterus was therefore removed by vaginal hysterectomy. The patient recovered and has remained well. The improvement in her condition has been most remarkable; she has gained flesh and her anæmia has disappeared. There is no evidence of recurrence up to the time of writing this paper (June, 1903).

The accompanying photograph, Fig. 1, is a representation of the uterus removed from this patient. The dark maroon colour of the growth was well seen on section. The uterus itself was plentifully supplied with blood vessels. Special care was taken during the operation to minimise the amount of blood loss, as the patient was already extremely anæmic.

MICROSCOPICAL EXAMINATION.

Low power. The muscular wall of the uterus is penetrated by strands of cells. The groundwork of the growth consists of a reticulated tissue containing in its meshes cells of different shapes. Multinucleated branching protoplasmic masses are seen. There is a considerable amount of fibrin and blood-clot in the specimen.

High power. The cells penetrating the muscular wall are found to be of three principal varieties: (1) Large cells with dark-stained nuclei rich in chromatin in which the cells' protoplasm is relatively clear; (2) smaller polyhedral nucleated cells; (3) irregular masses of multinucleated protoplasm of various sizes. In addition there is considerable infiltration with leucocytes. The reticulated tissue forming the groundwork of the growth is seen to contain in its meshes large rounded cells similar to those invading the muscular wall. In some of these the nuclei are undergoing division. There are also elongated cells containing one or more nuclei whose fusion may result in the formation of the multinucleated cell masses. The smaller polyhedral cells are now more apparent.

Numbers of large branching multinucleated masses are observed throughout the sections. Their nuclei are scattered irregularly in the cell protoplasm, and are deeply stained. The protoplasm in some of the cell masses is coarsely granular, and exhibits vacuoles, whilst in others granules cannot be seen, the protoplasm being either homogeneous or exhibiting slight linear marking. The abundance of blood-clot is a marked feature in all the sections.

CASE 2. Mrs. W., aged 46 years, was admitted into the Samaritan Hospital under my care on March 19th, 1902. She was an extremely anæmic, sallow-complexioned woman.

History. She had had six children, the youngest being nine years of age. She never had a miscarriage. Her menstruation was regular and scanty, lasting only two days. In August, 1901, she had an attack of bleeding, clots and fluid blood being passed *per vaginam.* This hæmorrhage ceased and did not recur until the end of December, 1901. After this date there was daily loss of blood from the vagina. A fortnight previous to her admission she was examined by a doctor and afterwards she stated that the discharge became fœtid. She had very little abdominal pain, but with the onset of hæmorrhage she had considerable pain in the sacral region.

Her mother died aged 67 years of "something in the liver." Father died aged 77 years. No definite family history of malignant disease could be obtained.

State on examination. She was well nourished and stated that she had gained flesh. Her anæmia, however, was extreme, the mucous membrane being pallid. Dyspnœa, on exertion, was marked.

Abdominal examination revealed a central swelling reaching to the midpoint between the umbilicus and the symphysis pubis, movable and painless.

Vaginal examination. A brownish, watery, extremely offensive discharge issued from the vagina. Bi-manually the swelling above noted was found to be uterine and of the consistence of a soft myoma.

I decided to make an attempt under anæsthesia, to disinfect the uterine cavity. Her temperature varied between 100°F. and 102°F. with corresponding depressions. On March 26th, she was anæsthetised, and on introducing the finger into the uterine cavity (which did not require preliminary dilatation) the walls were found to be covered with irregular nodules readily breaking down. Several necrotic pieces came away on withdrawing the finger. One portion was preserved for microscopic examination, but owing to the extent of the necrosis the sections were unsatisfactory.

The vaginal walls were carefully examined and high up on the anterior wall a bluish nodule was detected, flattened and commencing to necrose on its surface. Its size corresponded to that of a sixpence. As this was obviously a secondary growth no operation was attempted. Douching was employed and the patient was returned to bed.

By the aid of douching and careful nursing her condition improved so much that she was able to leave her bed on April 15th. However, towards the end of that month her temperature began to rise higher, accompanied by increased weakness. The temperature was never below 99°F. During the night of May 13th, a large quantity of discharge and dêbris was passed from the vagina, followed by a sudden fall in the temperature to 97°F. The temperature remained about normal for three days, but the general condition of the patient was much worse. She began to suffer from increasing dyspnœa, and the physical signs led me to suspect secondary growths in the lungs. The distressed breathing daily increased, and she died on May 23rd, 1902.

A *post-mortem* examination was made the following day by Dr. Bosanquet.

Abdominal cavity. Peritoneal cavity normal, no peritonitis or free fluid. Uterus enlarged and adherent to neighbouring coils of intestine. A few enlarged glands along aorta at pelvic brim, whitish in colour, largest about the size of a cherry-stone, soft, not visibly affected with malignant disease

Liver. Large, 4 lbs, fatty and congested. *No secondary deposits.* Gall bladder contracted, no gall stones.

Spleen. 5 oz., pale, tough. No sign of disease.

Kidneys. Right, 5 ozs.; left, 6 ozs.; pale, fatty, much fat in pelves. Capsules strip readily, surface smooth.

Adrenals. Normal.

Pancreas. Large, otherwise normal.

Stomach and Intestines. Much distended, no disease.

Uterus. Much enlarged, measuring about 4 inches vertically. Os patulous, easily admitting gloved finger which penetrates into a large cavity filled with blackish, somewhat offensive material. The uterus is practically converted into a thin-walled sac. At one point the wall ruptured on handling the organ, thus allowing the black contents to escape. Ovaries and tubes appear free from disease.

Thorax. Some adhesions in both pleural cavities due to masses of new growth in the lungs which have formed adhesions to the parietes. The lungs are studded with nodules of new growth, mostly cherry-red in colour. Some slightly umbilicated, most of them scattered indifferently about the lungs, but in places contiguous portions of the adjacent lobes are affected, some being adherent, others apparently separated by pleura. The largest nodule of growth is situated at the apex of the right lung somewhat anteriorly, and is 2 inches × 1½ × 2 in dimensions. The other nodules vary in size, from that of a pea to masses 1 inch in diameter.

On section the growths are reddish in colour, somewhat mottled, and in several of the nodules beside the reddish mass is a small nodule of a brownish-grey colour, the nature of which is not apparent without microscopical examination.

The bronchial and cervical lymphatic glands and the thyroid are not apparently affected.

Heart. Weighs 12 ozs., substance rather pale, valves and orifices normal.

Microscopical Examination.

Lungs. Numerous sections were cut from the secondary nodules present in the lungs. In the majority of these only blood and fibrin could be observed, although care was taken to obtain preparations which included the margin of the nodules. In a few, however, some rounded nucleated cells were demonstrated. None of the sections showed protoplasmic masses.

Vagina. No cellular structure was found in the preparations made from the secondary nodule in the anterior vaginal wall. The entire specimen was composed of fibrin and blood.

Uterus. Low power. Sections made from the wall of the uterus when examined under a low power show that the uterine muscle is penetrated by rounded cells with large nuclei, and also by irregular elongated masses of protoplasm. There is marked infiltration with leucocytes, and abundance of fibrin and blood-clot.

High power. The rounded cells above mentioned are seen to be large in size. Their nuclei, rich in chromatin, stain deeply, whereas the surrounding protoplasm absorbs the stain to a lesser degree. Similar cells exist in large numbers in all the specimens, and invade the uterine muscle in different directions. Some elongated "oat-shaped" cells tapering at both ends and possessing a dark-stained central nucleus are scattered throughout the specimen. In addition smaller polyhedral nucleated cells are seen.

The elongated protoplasmic masses appear to be broken up in all the specimens; some contain nuclei, others do not. This may be a degenerative change which has resulted in their distintegration, or may be due to the advanced stage of the disease.

Many of the muscular fibres of the uterus are swollen and œdematous. This effect is doubtless produced by the necrotic changes occurring in the growth. The marked infiltration with leucocytes is an evidence of the surrounding inflammatory reaction. No structure corresponding to a villus can be detected.

On studying these cases it must be admitted that the patient in Case 1 may have had a miscarriage, although her own evidence and that of her medical attendant was against this assumption. In the second case and in that already reported in the March (1903) number of this JOURNAL the occurrence of a recent pregnancy was not proven.

It seems, therefore, that in order to explain the incidence of the disease in the two last cases we must invoke the assistance of the theory that some fœtal relics had remained *in utero*, and had formed a starting point for the new growth.

Although the origin of the new growth from the coverings of the villi has now been conclusively demonstrated in many cases, I think it is well for the present to retain the title "deciduoma malignum," for under this term we can include not merely cases in which the origin of the disease may be directly proved, but others in which the proof is not complete.

Cases of "deciduoma malignum" have been in the past described either as sarcomata or carcinomata, but the more accurate pathological investigations employed at the present time, together with the interest aroused in the elucidation of this disease, have been the means of identifying many examples which had been placed in museums and labelled cancer or sarcoma.

The occurrence of six cases of "deciduoma malignum" at the Samaritan Free Hospital within the last three years has made me doubt the excessive rarity of the malady, and I feel sure cases will be more frequently reported in the future.

It is probable, too, that the degree of malignancy has been overestimated. This is doubtless subject to considerable variation, some types exhibiting excessive malignancy, whilst others, especially the polypoid or circumscribed types, show this character to a lesser degree. Case 1 is an example of what may be termed the polypoid or circumscribed type. Case 2 represents the diffuse type in which the growth is diffused throughout the uterine mucous membrane, whilst the case previously reported in the March number of this JOURNAL furnishes yet a third type where the uterine cavity is filled with blood clot, and may be described as the "hæmorrhagic type." Examples of the last have been recorded under the title of sarcoma teleangiectodes, cavernous or angio-sarcomata of the uterus, and

Fig. 1.

have all been characterised clinically by the occurrence of most profuse hæmorrhage with considerable accumulation of blood and clot *in utero*. They appear to be comparatively rare.

Considerable interest attaches to cases in which the secondary deposits are alleged to have disappeared. If this be fully proved then we are justified in dealing surgically with cases in which secondary nodules exist in the vagina, unless the general condition of the patient contra-indicates any operative interference.

Let me add in conclusion that if we are to solve the many important problems connected with this disease it will be by careful and accurate records of cases without having in view the support of any theory as to the causation.

Description of Figures.

Fig 1 is a reproduction of a photograph of the uterus in section (natural size). (Case I.)

The growth, which was covered by intact smooth mucous membrane, was assuming a polypoid shape.

The irregularity apparent at the lower part of the growth was caused by manipulations during the digital exploration.

The growth is seen to invade the uterine wall, whilst the wall itself is hypertrophied.

On section the growth was of a dark maroon colour owing to its vascularity, and was extremely soft in consistence.

Fig. 2. The photograph represents the uterus and vagina removed post-mortem.

The cavity of the uterus has been laid open to show the irregular nodulated condition of its interior. The growth is diffused over the whole of the inner surface, and has penetrated into the muscular wall of the uterus. As a result marked thinning of the uterine substance has been produced so that perforation occurred at one point during the removal of the organ from the body.

Under the mucous lining of the anterior vaginal wall a "secondary nodule" is seen.

Fig. 3. Represents a portion of a lung from the same patient, showing "secondary deposits" in the pulmonary substance.

REVIEW OF CURRENT LITERATURE.

OBSTETRICS.

Child-bed in Mothers under 16 years.

PICARD (GEORGES). *Revue Pratique d'Obstétrique et de Paediatrie*, April, 1903.

THIRTY-EIGHT cases of labour in patients under 16 years of age are analysed by the author. Menstruation in these cases had become established at an earlier age than is usual in France, varying from 10½ to 14, the average being 12 years. No special development of pubic or axillary hair was noted; in the case of a primipara of 14, a marked increase of the growth of hair occurred during her three month's stay in hospital. Very little was noticed in the way of complications during pregnancy. Digestive troubles, hæmorrhages and albuminuria were all insignificant. Eclampsia has been stated to be most common among young primiparæ, and this has been ascribed to the frequent presence of albumen in the urine. No case of eclampsia occurred, and albumen was found only in the urine of one patient, and then on but one occasion. There was no instance of mania or other affection of the nervous system. It has also been asserted that these patients are more prone to premature confinement; 29 of these cases went to term, 9 were prematurely delivered, and in 2 of these the fœtus had died *in utero*. All presentations were of the vertex, 25 were L.O.A., 12 R.O.P.; in 11 cases out of 18 in which examination was made some time before delivery, the head was found not to have engaged.

The length of the first stage varied from 22 hours to 3½, the average being 11 hours; the average duration of the second stage was 1¼ hours, and of the whole time of delivery 14¼ hours. Delivery was spontaneous, except in one case where intervention was required to extract a dead child from a mother with a contracted pelvis. Rupture of the perinæum was unusual; in three cases only did this occur, and all were quite trifling lacerations. Nothing remarkable was noticed in the third stage (in one case artificial delivery of the placenta was necessary), or in the puerperium.

The weights of the infants of these young primiparæ showed no divergence from the usual figures; 17 weighed between 3·25 and 3·9 kilos, 7 between 3·0 and 3·2, 5 between 2·5 and 3, and 9 weighed less

than 2·5 kilos. The infants were not under observation long enough to permit of a definite statement as to their progress, but they did not appear to increase in weight as regularly as other children during the early days of their life.

The results of this study of child-birth in very young mothers do not suggest any difference from that in primiparæ in general.

JOHN S. FAIRBAIRN.

Some Observations on Retrodeviation of the Pregnant Uterus.

POUEY (H.). *La Gynécologie*, April, 1903.

AFTER Doléris's interesting article on the surgical treatment of retroversion of the pregnant uterus, Pouey thinks it an opportune time to publish his own observations on this subject. His experience is that surgical treatment is not indicated even when on the first examination the uterus appears to be absolutely irreducible. Up to the present he has always been able to avoid operative treatment. If firm adhesions exist there is usually sterility owing to disease of the appendages.

Rest in bed, with attention to micturition and defæcation is usually sufficient. In every case attempts at reduction should be made every other day or at longer intervals if the lower abdomen is tender after manipulation. The first attempt is seldom successful. The best position is the genupectoral, followed by Trendelenburg's position.

In many cases women with pre-existing retroversion go through pregnancy without bad symptoms.

CONCLUSIONS.

1. Simple retroversion of the uterus, if the cervix and appendages be healthy, offers only a slight hindrance to conception.

2. After delivery retroversion frequently recurs.

3. Pregnancy in a retro-deviated uterus frequently progresses normally without any need for interference.

4. In a small proportion of cases of pregnancy with retro-deviation of the uterus, incarceration occurs. In these cases, however, reduction by the aid of properly applied manipulations is usually if not always possible.

5. To be successful it is essential to reduce the retro-deviated uterus patiently by successive manipulations. Trendelenburg's position appears to be the best, but in some cases the genupectoral or dorso-lumbar positions are successful.

6. These manipulations are very well tolerated.

HENRY RUSSELL ANDREWS.

Intestinal Obstruction due to Compression by the Gravid Uterus.

Brindeau (A.). *Bulletin de la Soc. d'Obstét. de Paris.* No. 3. Meeting of March 19th, 1903.

A primigravida, near the full term, had suffered for some days from abdominal symptoms, supposed to be due to appendicitis. There were abdominal pain, vomiting (green) and rapid pulse (120). Neither fæces nor flatus had been passed for four days. The gravid uterus containing a living child occupied the whole of the abdomen; there was no marked intestinal distension; the abdomen was tender, particularly in the right iliac fossa.

The abdomen was opened in the right iliac region, and no sign of peritoneal inflammation was discovered; the intestines were slightly distended. The abdomen was closed and various sorts of aperient enemata were administered without the slightest passage of fæces or flatus resulting. As the vomiting continued and the general condition became more grave, Cæsarean section was performed and a living fœtus was extracted. The peritoneum was quite healthy, but the "pelvic colon was empty and retracted." Within a few hours of the operation flatus was passed, and the administration of an enema resulted in several copious actions of the bowels.

Both mother and child left the hospital in good condition.

G. Drummond Robinson.

The Artificial Rupture of the Membranes as an Aid to Labour.

Gibb (G.). *The Scottish Medical and Surgical Journal,* April, 1903.

The author records several cases in which he claims that he has greatly facilitated labour by the early rupture of the membranes. The value of this form of treatment in certain pathological conditions, as hydramnios and concealed accidental hæmorrhage, is first discussed, then follows a series of cases, in which this method of treatment has been employed where the cervix was unusually rigid, or the amount of peri-waters was deficient. The author continues: "I have endeavoured to show in the fore-going remarks that in a by no means inconsiderable proportion of the cases one meets in practice, a very manifest advantage is gained by a very simple proceeding; but the consideration of cases such as those I have cited, naturally opens up the question of the advisability of earlier rupture as a means of expediting labour in all respects normal. If the presence of the bag of waters is not so absolutely essential in

these somewhat abnormal cases as a dilatory force, is it not at least possible that its superiority over the solid head, as a dilating wedge may be lost long before the stage of full dilatation is reached? Labour, even when absolutely natural, is not such a pleasant process for the patient that we need unnecessarily prolong it, and if by any means we can shorten, and shorten with safety, her ordeal, we shall obtain her profound gratitude."

HERBERT WILLIAMSON.

Gonorrhœal Puerperal Fever.

TAUSSIG (F. J.). *American Gynecology*, April 1903.

TAUSSIG records five cases of puerperal infection in which the gonococcus was found bacteriologically in the discharges, and discusses the clinical features and treatment of gonorrhœal puerperal fever. Although almost invariably secondary to a gonorrhœal process elsewhere, it must be classified under the head of puerperal fever, as it involves an infection of puerperal wounds. The gonococcus is the etiological factor in about $\frac{1}{6}$th of all cases of child-bed infection; it may gain access to the uterine cavity without any internal examination being made, and in this way many of the cases of so-called autogenous infection may be explained. More frequently, however, the process is brought about by digital examinations and operative manipulations, particularly intra-uterine, in the delivery of the child and placenta. For the first five days after delivery there is usually no disturbance of any kind on the part of the mother, though a slight rise of temperature to 100·5° on the 3rd or 4th day is common. There is usually a slight increase in the pulse-rate, but on the whole the patient feels perfectly well, unless it be for some sensitiveness about the cornua of the uterus. As a rule the puerperium seems to run a perfectly normal course for the first six days. The lochial discharge is generally the first thing to attract attention; by the 6th day it has become very profuse, and has a peculiar, rather disagreeable odour, differing from the foul smell of retained placental tissue, and also from the stale odour of normal lochia. It has a glairy appearance and tenacious character, from the large amount of mucus present, and its colour is more yellow than normal. It is also very irritating, often giving rise to considerable soreness about the wounds of the external genitals, and occasionally even causing an intertrigo. The first general evidence of an infection is shown about the 6th or 8th day *post partum*, by rigors, a temperature of 103°, and severe abdominal pains with tympanites.

The fever is usually of short duration and without the irregular rise and fall as in a streptococcic infection. The pulse is only slightly quickened—to 100 or 110— and is full and regular. In the cases where the first symptoms occur later, about the 12th to the 14th day, the attack may be so mild as to permit of the patient's being up and about, and may be entirely overlooked. That, in those cases in which the temperature begins to rise as early as the 6th day and runs up to 103° and 104°, the infection is not necessarily a mixed one as held by Bumm and others, but may be due to the gonococcus alone, was shown by two cases in the author's series, where cultivations from the uterine cavity proved to be pure growths of the gonococcus. A definite diagnosis can only be made by the discovery of gonococci in the lochial discharge.

Prophylaxis is of more benefit than treatment. All pregnant women, having gonorrhœa, should be delivered as far as possible without internal examination. Treatment should be limited to one or two intra-uterine douches, frequent vaginal irrigations, and rest in bed for a prolonged period of time. Curettement involves too much risk of a general infection. Local collections of pus in the pelvis will require vaginal incision and drainage.

JOHN S. FAIRBAIRN.

Hysterectomy in Puerperal Infection.

DOLÉRIS (J. A.). *La Gynécologie*, April, 1903.

DOLÉRIS is in agreement with the general opinion expressed by the Congress at Rome (1902), that hysterectomy is of very limited value in the treatment of acute puerperal infection. From a study of a large number of fatal cases during the last five years, he concludes that, as shown by the autopsies, two cases only could possibly have been saved by hysterectomy. In the other cases the lesions were multiple, and beyond the reach of any operative procedures. In some rare instances of the thrombo-phlebitic type of infection, as shown by repeated rigors, this operation must be seriously considered. The course of the infection is often slow, and for a time it remains limited to the uterus and broad ligaments, the appendages and peritoneum being only slightly infected. To these must also be added cases of putrid infections with placental retention, and also infected myomata. Doléris has recently had a case of this nature in which he performed hysterectomy, and he records the details fully in this contribution. The patient, a primipara, was first seen fifteen days after

delivery, and presented all the signs of a grave type of infection. The uterus was curetted, followed by *ecouvillonage* without any benefit. The uterus was much enlarged and softened, the broad ligaments infiltrated by exudation. The appendages were apparently normal. Hysterectomy was practised by the abdominal route, owing to the fixity of the uterus in the pelvis and its great friability. The pelvic peritoneum was united over the floor of the pelvis and a gauze vaginal drain inserted. The uterus showed all the signs of severe streptococcic infection; organisms could be seen filling the dilated blood-vessels. There was no collection of pus. The appendages were softened but apparently healthy and contained no organisms. Blood cultures carefully made were all sterile.

The patient, though very ill for a time, gradually recovered. The temperature fell to normal in a few days. Convalescence was delayed by some pulmonary congestion, and also by the formation of three subcutaneous abscesses, the sites of injections. In six weeks she left the hospital apparently well. A few days later she developed purulent pleurisy. Chloroform was given to evacuate the pus, and the patient died of syncope during the operation.

The *autopsy* showed that the right pleural cavity contained pus with numerous virulent streptococci. The lungs showed recent infarcts. A purulent focus was found in the abdominal wall, communicating by a sinus with the floor of the pelvis, which showed many dense adhesions. The left utero-ovarian pedicle contained an enormous thrombus, which, however, contained no organisms.

This case is of great interest. The patient was apparently cured by the operation, but the final result showed that although the vaginal focus of infection was entirely removed, the streptococci may remain virulent in the body for many weeks, and finally lead to a fatal termination.

Doléris concludes that this operation may be tried in cases of prolonged and remittent infection of the phlebitic type. In these cases the economy possesses a marked defensive power, and tends to limitation of the lesions. It is essential that the operation should not be delayed too long. He is, however, unable to give precise clinical evidence as to the period to undertake it, and the results must, with our present knowledge, be very uncertain.

Arnold W. W. Lea.

GYNÆCOLOGY.

The Ætiology of Ovarian Adenoma.

WALTHARD (MAX). *Zeitsch. für Gebürts. und Gynäk.*, Band xlix., Ht. 2.

THE author has examined 80 ovaries from all periods of life, including ten from newborn infants, and two from a patient aged 68. Each ovary was completely cut up into serial sections, and all the sections examined. The organs were, for the most part, normal, though insignificant cysts were now and again discovered. The result of this laborious investigation is embodied in a paper of about 100 pages, with the addition of 26 clear and well-executed illustrations.

At the outset one or two points in the normal histology of the ovary are dealt with. It is argued that the term "germ-epithelium" should only be employed until the end of the first year of extra-uterine life, because there is sufficient ground for believing that after the end of the first year no further ova are formed. After the epithelium covering the surface of the ovary has lost this faculty of producing new primitive ova it is better called simply ovarian epithelium or surface epithelium. The origin of the membrana granulosa is also discussed, and the author's observations have led him to an exactly opposite conclusion to Wendeler. The latter supports Foulis's theory of the origin of the cells of the membrana granulosa from the connective tissue stroma of the oary; Walthard, on the other hand, has convinced himself that the cells of this layer are derived from the germ-epithelium.

Further interesting questions in relation to the development of the ovary, have to do with the separation of the last solid bundles of ova from their connection with the surface epithelium, and with the division of the bundles of ova into primitive follicles. In this process it often happens that groups of cells, derived from the germ-epithelium but without ova, are found lying in the stroma of the ovary. These collections consist of two forms of cells, the more numerous of which are cubical, with clear protoplasm and clear vesicular nuclei, while between these, here and there, are intercalated cells (schaltzellen) with small, darkly-stained, angular nuclei. The groups have usually a rounded or oval form, and show a stage of growth followed by a stage of regression similar to the process known under the name of follicular atresia; to these groups of cells

the author gives the name "granulosa bundles." Collections of similar cells to those just described are sometimes seen, forming tubes, in some of which, either between the epithelial cells or in the lumen, ova are found; to these tubes the name granulosa tubes is given; their fate is the same as that of the granulosa bundles.

During the first years of life the remains of the bundles of ova separate from the surface epithelium, and the granulosa bundles and tubes, as well as many primitive follicles, undergo atresia. In the later years, until long after the climacteric, other groups of cells are found in and immediately below the surface epithelium, especially on the anterior surface of the ovary near the hilum. These cells contain round or oval, clear vesicular nuclei in clear protoplasm, and are markedly differentiated from the similar ovarian epithelial cells with small, darkly-stained nuclei. Sometimes they occur in small groups of three or four cells; in other places similar cells are found surrounding a small cavity, from which hollow processes lined by a single layer of cylindrical epithelium push out into the stroma; in this way long glandular tubes may be formed. Walthard considers that these cells are not derived from the granulosa bundles and tubes above mentioned, but are a kind of surplus surface epithelium.

Two kinds of glandular tubes lined by ciliated epithelium are also described as having been found both in the epithelium and in the stroma. They occurred either with or without the tubes lined by cylindrical epithelium just described, and the ciliated epithelium was only observed after puberty. In one variety small cysts, without any tendency to the formation of warts, were lined by a layer of cylindrical epithelial cells among which some were ciliated; the stroma round these tubes was not differentiated. In the other variety with similar epithelium branching papillæ were formed, and the surrounding stroma was richer in nuclei and stained differently to the rest of the stroma. Cysts of these kinds lined by ciliated epithelium were found in eight cases.

In addition to the various epithelial groups already mentioned, cell nests and glandular tubes with beaker cells and all the intermediate stages in their formation, were observed in six cases, and finally collections of squamous epithelium were seen occasionally. All these groups and tubes lie partly intercalated in the surface epithelium and partly in the stroma without any connection with granulosa collections or follicles. The author's observations illustrate the important fact that in the ovary not every collection of cylindrical, ciliated, or beaker cells lead to large tumours. He considers these collections of cells, ciliated, columnar or mucous, to be

congenital, and not derivatives of the surface or follicular epithelium.

Remains of the Wolffian body are found in the hilum of every ovary, sometimes with, sometimes without a wall of connective tissue and muscular fibres; the canals often show dilatations, in which the epithelium becomes low and flattened. An adenomatous arrangement of the Wolffian body with well developed epithelium in dilatations of the glandular tubes was only observed in one single ovary.

Every future worker in this field will have carefully to study this work. The admirable industry and characteristic German thoroughness with which the investigation has been made are worthy of the greatest admiration, and the author has succeeded in no small degree in giving a connected and intelligible account of the present position of a very difficult subject. That much still remains to be done is shown by the polar divergence of opinion that still exists in many parts of the subject, as for instance in respect to the origin of the cells of the membrana granulosa.

THOMAS WILSON.

Wolffian Relics in the Human Ovary.

WILHOSER. *Ueber Urnierenreste in den Adnexen des menschlichen Uterus.* Inaug. Dissert Zurich, 1900. Abstract in *Rev. de Gynéc. et de Chirurg. Abdom.*, March—April, 1903.

WILHOSER examined two ovaries from a seven months' fœtus, two from a child aged two, and sections of the ovaries of a girl aged fourteen. He found that traces of the Wolffian body were to be detected in three places near the ovary, the most important seat of these relics was the epoöphoron, which persisted and grew proportionately with the ovary proper. The paroöphoron, consisting of little canals placed between the folds of the mesosalpinx and mesovarium was less developed and atrophied sooner. There remained a third point where Wolffian relics were to be found, namely the medullary part of the ovary proper. The relics appeared as little canals derived from the glomeruli of the Wolffian body; they were distributed over an area varying in extent in different specimens, and they could proliferate.

The importance of Wilhoser's researches is evident. As he rightly concludes, the distribution of these relics must be taken into account in respect to the pathology of cysts and teratomata in the ovary and broad ligaments. Between 1880 and 1890 Coblenz, Bland-Sutton and the writer of this abstract maintained the Wolffian origin

of papillomatous cysts of the ovary and parovarian cysts on histological grounds, and also on the evidence of anatomical relations. The fact that papillomatous cysts burrow between the layers of the broad ligament, yet often involve the hilum alone, the oöphoron sometimes remaining distinct, is significant in relation to the frequency with which Wolffian relics have been found in the hilum. The development of papillomatous cysts occasionally in the oöphoron, the natural seat of glandular cysts, is accounted for by this theory, since Wolffian tubes sometimes stray into the oöphoron. Histologists should not overlook Harz's "Contributions to the Histology of the Ovary in the Mammalia," published in the *Archiv für mikroskopische Anatomie*, 1883 (vol. xxii., pp. 374—407). Harz detected perfectly developed ingrowths from the Wolffian ducts permeating the entire stroma in the ovary of the American monkey *Cebus*, the hare, guinea-pig and horse, the same was noted by him, but to a less extent in the marmozet, cat and ox. He could not find any Wolffian tubes in the ovary of the pig or in woman, but the present writer had detected, at the time that Harz's paper appeared, entire Wolffian tubes in the epoöphoron or tissue of the hilum of the human fœtal ovary.

Kossmann's theory endeavours to prove that broad ligament and papillomatous cysts are developed not from Wolffian, but from Müllerian relics, accessory tubes and accessory fimbriæ. It seems highly probable that free papilloma of the broad ligament may have its origin in Müllerian elements. But Wilhoser and Harz's researches strongly favour the older theory. Müllerian or Fallopian tube elements may conceivably penetrate into the hilum or the ovary proper in some cases, but Wolffian elements appear normally in those tracts and are therefore more likely to be the source of encysted papilloma.

ALBAN DORAN.

A Fibroid of the Uterus in a Girl of 13.

CAVAILLON (M. P.). *Lyon Médical*, June 15, 1902.

AN abstract of this case, taken from a report in the *Journal de Médecine de Paris*, appeared in the last number of this journal, in which considerable doubt was expressed as to its authenticity owing to the absence of any note of a microscopical examination of the growth. The account in the *Lyon Médical* is more complete, and from it, it appears that a histological examination was made by M. Bernard de Teyssier in the laboratory of Prof. Tripier, and the

tumour reported on as a fibro-myoma, so that the case must be accepted as a genuine example of a uterine fibroid occurring at a remarkably early age. Judging by the first appearance of symptoms the tumour was present when the patient was only twelve years of age.

JOHN S. FAIRBAIRN.

Salpingopexy.

FAURE (T. L.). *La Gynécologie*, April, 1903.

SUSPENSION of the Fallopian tubes to the side of the pelvis does not appear to have been practised hitherto, but Faure believes that this may prove very useful in certain cases.

The patient upon whom he carried out this procedure was suffering from adherent retroflexion of the uterus with prolapse of the apparently healthy tubes and ovaries. The adhesions of the uterus to the rectum and pelvic floor were very dense. They were separated by scissors and the uterus brought forward. The appendages still tended to prolapse. Faure, therefore, united the outer third of the Fallopian tube to the peritoneum of the infundibulo-pelvic ligament at the side of the pelvis. The appendages thus remained suspended at the level of the pelvic brim, and have since shown no tendency to fall again into the pouch of Douglas. They further help to maintain the uterus in good position

Faure points out that after abdominal operations there is a great tendency for the appendages to prolapse by their own weight into the pouch of Douglas, and even to again become adherent. He is of opinion that this method of suspension, which is so easy to carry out, and does not interfere with the movements of the fimbriated extremity of the tube or the ovary, will be found of great value.

ARNOLD W. W. LEA.

Changes in the Vermiform Appendix Observed During Gynæcological Operations.

HERMES. *Deutsche Zeitsch. für Chirurgie.* Bd. lxviii., Ht. 3 and 4.

THE author of this paper records the results of an examination of the appendix in 75 laparotomies performed for disease of the female pelvic organs. The cases are reported in a table showing the age

of the patient, the number of pregnancies, the operation performed and its result, and the state of the appendix. In 40 cases, or 53·3 per cent., the vermiform appendix was found affected in some degree and removed. No relation could be made out between the age of the patient or the number of pregnancies and the occurrence of changes in the appendix. The cases in which its removal was found necessary were as follows:—

In 22	cases of	tubal pregnancy	it was	affected in	8 or 36·4%
„ 20	„	pyosalpinx	„	„	11 or 55·0%
„ 16	„	chronic disease of the adnexa	„	„	11 or 68·7%
„ 11	„	ovarian cyst	„	„	6 or 54·5%
„ 6	„	myoma uteri	„	„	4 or 66·6%

The changes observed in the appendix are divided into two groups: (1) where the mucosa is chiefly involved, with abnormal contents of the canal as muco-pus or pus, or fæcal concretions; (2) where adhesions to the surrounding organs or pelvic wall form the principal feature. In the case of the first group the disease is evidently unconnected with that of the genital organs. This was noted in 11 cases, *i.e.*, in 14·7 of all the cases disease of the appendix was discovered at operation as an independent affection, and without having given rise to symptoms calling attention to it. In the case of the second group, the author discusses three possibilities: (1) that the disease may be primary in the genital organs; (2) that it may be primary in the appendix; and (3) that the two may be independent, and comes to the conclusion that the first of these is the most frequent occurrence. He therefore advises that the appendix should be carefully examined in all cases of laparotomy for pelvic disease, and removed, if affected, unless some special contraindications are present.

In his series, 6 cases out of the 75 were fatal, and in 4 of these the appendix was normal. Of the 2 in which it was removed, the cause of death was directly traceable to this operation in one, giving a mortality of 1·3 per cent., and doubtless this percentage would be reduced in statistics covering a larger number of cases.

JOHN S. FAIRBAIRN.

NOTE.—*The Index Obstetricus will in future appear quarterly, and will be classified in a form which we hope will make it of greater service to our readers for purposes of reference.*— EDITOR.

REPORTS OF SOCIETIES.

OBSTETRICAL SOCIETY OF LONDON.

Meeting, Wednesday, June 3rd, 1903, the President (Dr. Edward Malins) *in the Chair.*

Dr. John H. Teacher read a paper on

Chorionepithelioma and the Occurence of Chorionepitheliomatous and Hydatidiform Mole-like Structures in Teratomata.*

The paper was illustrated by specimens and an epidiascope demonstration.

The following series of specimens was also exhibited at the meeting:—

1. Lieut.-Col. A. Sturmer (Madras): Uterus removed from a Hindu woman by vaginal hysterectomy, two years after labour.

2. Dr. F. W. N. Haultain (Edinburgh): Uterus removed by vaginal hysterectomy for chorionepithelioma six months after passage of a vesicular mole, 1898. Patient well in 1903.

3. Dr. Horrocks: Deciduoma Malignum without Syncytium. Death eight months after passage of a vesicular mole.

4. Dr. Briggs (Liverpool): Two specimens of Chorionepithelioma.

5. Dr. Thos. G. Stevens: Chorionepithelioma five months after passage of a vesicular mole. Vaginal hysterectomy. Death in three days.

6. Dr. J. M. Munro Kerr (Glasgow): Chorionepithelioma following abortion; September, 1901. Curetted March and May, 1902. Then vaginal hysterectomy when diagnosis was made.

7. Dr. F. W. Andrewes: Endosteal Sarcoma of Femur, showing syncytial structures.

8. Dr. Herbert Williamson: Syncytioma of Uterus from a patient, who died three years ago at St. Bartholomew's, 15 months after passage of a vesicular mole. Secondary growths (?) in lungs, liver and vagina.

9. Dr. T. A. Helme (Manchester): Chorionepithelioma of Uterus and Metastatic Growths in Lungs.

10. Dr. James Ritchie (Oxford): Embryoma of Anterior Mediastinum from a male, aged 24, with secondary tumour in lungs.

11. Dr. Cuthbert Lockyer: Chorionepithelioma of Uterus with Vaginal, Parametric and Pulmonary Metastases. Secondary growth appeared in labium two months after labour.

12. Dr. Herbert Spencer: (1) Chorionepithelioma of Uterus, Cervix and Lungs. (2) Case observed in Great Britain in 1889, published in France 1895.

13. Dr. Russell Andrews: (1) Chorionepithelioma of Uterus. Specimen from London Hospital labelled cancer, etc., and in museum for many years. (2) Chorionepithelioma in Uterus and Vagina in woman aged 50, whose last confinement was 11 years before. Metastases in lungs.

14. Dr. W. H. Tate: Chorionepithelioma of Uterus removed by vaginal hysterectomy, following abortion 18 months previous.

*This Paper will be found on page 1.

15. Dr. F. J. McCann: (1) Chorionepithelioma of Uterus with secondary deposits in vagina and lungs; aged 46. (2) Chorionepithelioma of Uterus removed by vaginal hysterectomy in 1901; patient remains well. (3) Chorionepithelioma in woman of 53 years of age.

16. Dr. Galabin: (1) Myxoma of Fundus Uteri following passage of a vesicular mole, curetted four times; patient was well ten years later. (2) Vesicular Mole, showing syncytium partially differentiated into cells. (3) Carneous Mole, exhibiting prolonged vitality of chorionic villi without malignancy.

Discussion.

Dr. Peter Horrocks considered the paper a valuable piece of work and an important contribution to the solution of a vexed question. It was necessary, however, to correct the statement that this Society had some years ago come to a conclusion on the matter. As a fact, the Society never did come to conclusions. The opinions of individual Fellows did not commit the Society as a whole, and at the discussion referred to by the author, so far from the views expressed by the late Dr. Kanthack and Dr. Eden and others being accepted, the records of the Society would show that such was not the case. Specimens had been shown and discussions had been held upon them indicating a variety of opinion. As recently as January, 1902, Dr. Lockyer had shown a specimen and had stated his opinion that there were two kinds of malignant growth associated with pregnancy, one a mesoblastic sarcoma of decidual, and, therefore, maternal origin, and the other a syncytial carcinoma or chorionepithelioma, and, therefore, of fœtal origin. Dr. Lockyer stated that the malignant sequela of the vesicular mole was invariably a syncytioma. Now, to-night, he (the speaker) exhibited a specimen, which seemed to prove that this statement was incorrect.

The patient came under his care at Guy's Hospital, when his colleague, Dr. Galabin, resigned his position. The woman was moribund and only lived a week or two afterwards. She began bleeding during a pregnancy in the early part of 1902, and then was delivered of a vesicular mole. The bleeding stopped, and she menstruated normally three times before bleeding set in, which it did in November, 1902. When she came into the hospital, she had extensive cancer in the uterus, which reached as high as the navel, in the vagina from which nodules protruded so as to be visible, and in the lungs, giving rise to hæmoptysis.

At the post-mortem examination the usual condition of things was found. But the chief interest in this specimen lay in the fact, that in spite of this being a genuine case of a sequela of hydatidiform degeneration of the chorion, yet no syncytium could be found in the growth nor in any of the secondary growths. Both had been carefully examined by his colleagues, Mr. Targett and Dr. Hicks (the Obstetric Registrar at Guy's). The specimen was shown and also microscopical sections, and the characteristics were more those of sarcoma than of carcinoma. One point was to be well noted, namely, that the woman menstruated normally three times after passing the mole, whereas, in most cases, the patient never really got well after delivery, but kept on losing more or less as the disease progressed. Still it was a sequela, but whether *post* or *propter* he could not say; only it must no longer be alleged that this form of growth following hydatidiform mole was invariably a syncytioma.

Again, in 1901, he had shown a specimen of so-called "deciduoma malignum" at that Society, removed from a woman who was sent into

Guy's with a history of miscarriage with subsequent hæmorrhage, and she was operated on with the idea of removing retained products of gestation. At the operation, it was discovered that there was a growth in the body of the uterus, and so vaginal hysterectomy was done, and the patient recovered. But this specimen was submitted to the Pathological Committee of the Society, and whilst fully agreeing that it was a typical syncytioma, they expressed their doubt as to their being any evidence of a recent pregnancy. She was 47 years of age, and the history of miscarriage was by no means conclusive. She had a flooding and thought it must be an early miscarriage, but it was doubtful whether she had missed a period, and there was nothing in the nature of an ovum ever seen. Hence, if it were assumed that this woman had not been pregnant recently, here you got a typical chorio-epithelioma, or a syncytioma with no fœtal or ovular origin.

He did not feel that we were in a position yet to state that all these cases were of maternal or of fœtal (ovular) origin. Indeed he felt inclined to believe with Dr. Lockyer and others that there were two kinds of malignant growth associated with pregnancy, one of decidual (maternal) origin of a sarcomatous type, for which the term "deciduoma malignum" was appropriate, and the other a chorio-epithelioma of fœtal (ovular) origin of a carcinomatous type.

But he would like to ask two questions:—

(1.) Were all malignant tumours of the uterus that contained syncytium, following and associated with a pregnancy, *ipso facto*, of fœtal (ovular) origin, that is, did the presence of syncytium prove ovular origin?

(2.) Was it possible for a malignant growth associated with pregnancy to be of fœtal (ovular) origin, and yet to be of the sarcomatous type without syncytium, or were all such growths of decidual or maternal origin?

Dr. Haultain thanked Dr. Teacher for his admirable communication, which, from its completeness, would stand as a classic on the subject in the English language. Although, as Dr. Horrocks had said, the Obstetrical Society did not commit itself as a whole to the opinions expressed in the discussion of 1896, yet the individual members, without exception, committed themselves to the sarcoma theory, and naturally this was accepted by the continental observers as the expression of British opinion, no other discussion of the subject having been published.

In 1898 a case of so-called deciduoma malignum had come under his care; this was cured by vaginal hysterectomy, and the woman was still well. In consulting the literature at that time, he was much struck by Dr. Teacher's paper, describing Dr. Kelly's case, and on investigating the subject for himself, he had at that time absolutely adopted the view promulgated by Marchand, namely, the new growth in question was epithelial, and ovular in origin. Since then he had become more and more convinced of the correctness of that view, and absolutely concurred in what Dr. Teacher had stated. When he presented his paper before the British Gynæcological Society in 1899, the general trend of expert opinion was just commencing to turn towards the adoption of the ovular origin, which was now very generally accepted. Everything pointed in this direction, the similarity of the cells of the growth to those of the chorionic coverings, and the frequency of the occurrence of the new growth after hydatidiform mole, which in itself was due to marked proliferation of Langhans' cells and the syncytium. It seemed to him there was no weak link in the chain of evidence. From the completeness of

Dr. Teacher's demonstration, it was unnecessary, after stating complete concurrence, to enter further into the pathology, but clinically there were one or two points of importance he should like to mention.

As regards the indications for radical treatment by hysterectomy, the simple demonstration of syncytial masses in uterine scrapings was not sufficient, particularly after the expulsion of a mole, as portions might be retained without assuming malignant action, and could be cured by curettage, as he had twice seen. When, however, violent hæmorrhage was associated with the curettage the prognosis was much more unfavourable, and the cavity of the uterus should be at once explored by the finger for the detection of a growth. He was much interested in the cases of spontaneous cure after metastases. This might be accounted for by the tendency of the growth to kill itself by the free extravasation of blood, choking cell growth, the particular rôle of these cells being to penetrate blood-vessels and flourish in the circulating blood-stream.

Dr. T. Arthur Helme (Manchester) expressed surprise at the sweeping character of some statements in the paper. He had understood Dr. Teacher to say that no case was on record that supported the sarcomatous nature of these tumours, and that no "deciduoma" with solely sarcomatous tissue had been recorded, that all these tumours are chorionepitheliomata, and that he had never seen maternal tissues growing after a fashion at all comparable with the cells of these tumours. In order to clear the way for these opinions Dr. Teacher ruthlessly brushed aside the maternal origin of those tracts of cells which are to be found in the intervillous spaces, and which we have looked upon as "decidual" (maternal), and boldly said that they were all of trophoblastic or ovular production. In support of this he (the speaker) had failed to hear any evidence adduced by Dr. Teacher except the similarity of appearance of the cells, an unsafe basis of opinion, and a drawing, one of Dr. Haultain's preparations, which had been shown upon the screen; this drawing had been "made in Germany," and doubtless the artist had unconsciously allowed his imagination to tinge his product with the ideas which he wished to represent; that was not sufficient evidence for the important statement made. He (Dr. Helme) had brought to the meeting a specimen of "deciduoma" which had occurred in his practice some three or four years ago, but had not been recorded as on examination he had found that it supported the prevailing opinion that these tumours might be of "decidual" origin.

On hearing Dr. Teacher's opinion of the impossibility of such an origin he thought the specimen might be of some value, and though in the short time at his disposal he could not do the case justice, he would briefly allude to it and report the case more fully subsequently. Dr. Helme then gave a brief history of the clinical symptoms and appearances. At the *post-mortem* the tumour in the uterus was found, with metastases in ovary, vagina, vulva and both lungs. The microscopic appearances of *all* the growths, primary and metastatic, were *identical;* tracts of huge cells, evidently of short life history, with larger necrotic areas, wide blood-spaces, hæmorrhages, and fibrinous deposits; the cells, he supposed, Dr. Teacher would claim as the offspring of the cells of Langhans' layer, but he thought they were of decidual origin. He had been unable to find any of those spreading protoplasmic masses characteristic of the syncytium.

Some years ago he had made observations upon the histology of the pregnant and puerperal uterus (especially in the rabbit), and if one thing had impressed him more than any other it was the enormous hypertrophy which the maternal connective tissue cells underwent, and he would call

Dr. Teacher's attention to those huge plasmodia of maternal origin which were to be found not only in the uterine but also in the vaginal tissues. Shortly, he might state that the tumour which he now exhibited resembled in its broad features the sarcomata, but at the same time possessed special characters which demanded that it should be placed in a special class for which the name " deciduoma " seemed eminently suitable. He claimed that this specimen showed the possibility of the decidual, *i.e.*, connective tissue origin of some at least of these tumours.

As to the chorionepitheliomata the theory that we had differentiated in the chorion a stratum of tissue which is neither fœtal nor maternal and which was capable of giving rise to a malignant growth in its host, which was neither sarcomatous nor carcinomatous, was fascinating, but before accepting a doctrine which would so completely affect our views as to the origin of tumours we should demand explicit proof, and it seemed to him that this would not be forthcoming until it was demonstrated that what we had considered to be cells of maternal (connective tissue) origin were really of trophoblastic origin and until the source of the syncytium itself was identified.

Dr. F. W. Andrewes expressed his agreement with the main thesis of Dr. Teacher's paper, viz., that the tumour formerly known as deciduoma malignum is of fœtal origin and derived from the chorionic epithelium. He was, however, of opinion that the term " syncytioma " was preferable to chorionepithelioma as being less cumbrous and expressing the striking histological feature of the growth without implying any theory of its origin. The term chorionepithelioma also tended to suggest a relation to the carcinomata which Dr. Teacher was anxious to avoid. He referred to the great theoretical importance of admitting the fœtal origin of the growth pointed out by Adami, inasmuch as the invading cells were derived from another organism and rendered the assumption of an adventitious infecting microbe unnecessary.

With regard to those syncytial tumours of the uterus which appeared to have no connection with a pregnancy, he was of opinion that the ground was much less certain; the supposed teratomatous origin of such growths required careful scrutiny. It was necessary to show that an aberrant included ovum might actually give rise to chorionic structures, and to find syncytial tumours arising in connection with undoubted teratomata.

Until the present meeting he had never seen such proof. Both sarcoma and squamous-celled carcinoma might originate in dermoids, but Dr. Ritchie had shown that evening a syncytial tumour arising in a dermoid of the mediastinum in the male. Dr. Andrewes thought this the most important of the many valuable specimens shown at the meeting, but it was a rarity, and more such cases were needed to establish Dr. Teacher's position. It was not shown that these rare cases of syncytial tumour of the uterus, in which a pregnancy could be excluded, were so absolutely identical with the ordinary form that it was needful to invent an included ovum to explain them.

The acceptance of the view that ordinary syncytioma malignum is of chorionic origin does not compel us to accept such an origin for every syncytial tumour. Syncytial sarcoma is not a very rare thing. (Two specimens of mixed celled endosteal sarcoma of bone were shown under the microscope, containing immense syncytia, almost comparable with those of chorionepithelioma.) Might not the rare cases of syncytial uterine growth having no connection with pregnancy be perhaps of this nature? Such a

possibility was an additional reason for preferring the term syncytioma to chorionepithelioma.

Dr. Ritchie (Oxford) described the case of a young man, reported fully on p. 65 et seq., suffering from a malignant tumour of the anterior mediastinum of three months' duration with secondary growths in the lungs. He considered that this tumour was to be looked on as a teratoma developed from an included ovum, the part of which corresponding to the trophoblast had developed in a manner analogous to that part of the trophoblast from which an ordinary chorionepithelioma may arise. He would welcome, however, the discovery of other similar tumours as the possibility of the dermoid part of the tumour having arisen from an epithelial inclusion from the third branchial cleft might be advanced. In such a case the malignant part of the growth might be looked on as an angio-sarcoma of an accidental association. He had, however, never seen any instance of those tumours usually classed either as angio-sarcomata or endotheliomata, which at all resembled a chorionepithelioma.

Dr. W. E. Fothergill (Manchester) said that several questions had occurred to him during the reading of Dr. Teacher's most admirable and interesting paper. The author had defined the so-called *chorio-epithelioma* as a tumour of the uterus occurring in connection with pregnancy. Would it be possible to retain this definition and at the same time to continue to include under the name *chorio-epithelioma* (1) growths occurring in the female, but leaving the uterus perfectly healthy, and (2) growths occurring in the male subject? The neoplasm in question had now been described as occurring in (*a*) the male subject; (*b*) the young female apart from pregnancy; (*c*) females suspected of recent pregnancy; (*d*) females known to have been pregnant recently; (*e*) elderly females not suspected of recent pregnancy. In the case of, for instance, a female with a problematic pregnancy followed by a "syncytial" tumour in the vagina, how would it be possible to say whether the growth was due to pregnancy or not?

Was it proved, as Dr. Teacher had asserted, that the trophoblast was a distinct histological entity? Could its presence be detected infallibly by inspection, and could a new growth derived from trophoblast be recognised as such?

The speaker understood Dr. Teacher to have remarked that cases in which actual chorionic villi were observed had a more favourable prognosis than those in which no villi could be found. Did not this clinical observation suggest that the cases investigated formed two categories? Might not the more serious be instances of new growth causally connected with pregnancy, the less severe being examples of more or less pronounced invasion of the maternal organism by chorionic villi?

Dr. Teacher held that none of the cases reported gave any support to Veit's view that villi might be included with masses of new growth of maternal origin. Would it not, however, be easy to write descriptions of any, or indeed of all, the published cases in such a manner as to support Veit's theorem? Dr. Teacher further considered Veit's view to be finally negatived by the demonstration of certain changes in the walls of blood-vessels whose lumina contained chorionic elements. But could not similar changes in the walls of vascular structures be demonstrated in certain angio-sarcomata quite apart from the presence of chorionic structures? The above questions were some of those which had occurred to the speaker, but he had risen mainly in order to point out that the authors of certain papers referred to by Dr. Teacher appeared to have ignored the work of the late Dr. Kanthack and of Dr. Eden. For these

gentlemen had long since pointed out the similarity between the so-called chorionepitheliomata and other neoplasms, more especially certain growths of the testis. In the year 1896 they argued as follows:—The testicular and other neoplasms in question are sarcomata; therefore, until conclusive evidence to the contrary is produced, we prefer to regard the similar growths of the uterus as being sarcomata also.

At the present time our attention was again being called to the similarity between the various neoplasms in question, but in the opposite sense. The uterine growth we were now supposed to have accepted as chorion-epitheliomata, therefore the similar growths of the testis and other organs we were told must also be chorionepitheliomata. Eden and Kanthack had argued from the fairly well known to the unknown. The more recent authors had reversed the process; for it had by no means been proved that the growths in question were genuine embryomata. Granting that they were embryomata, the speaker thought that, if only out of consideration for the student of the future, care should be used in applying the same name to things so different as a chorionic growth affecting the mother, and an embryoma in a male subject. The theory expounded so clearly by Dr. Teacher was so simple and so attractive, one might say so fascinating in character, that it was sure to be accepted as a working hypothesis by all but the most sceptical critics. But, granting that all the growths in question were of ovular—of trophoblastic origin; would it not be well to adopt a nomenclature which would distinguish clearly those connected with pregnancy from those arising independently of that state? It was clear that a mother fatally invaded by the trophoblast of her own child would be a person of one generation killed by a tumour belonging to a person of the next generation—matricide, in fact. But a man slain by an embryoma in his testis would be a victim not of his own child, but of a potential brother or sister—a case of fratricide—a very different matter, and one worthy of a different name. It was easy to say that an individual had a trophoblast, be he your child or your brother, but the statement would not be easy to prove. We were aware that a trophoblast was essential to the implantation *in utero* of certain mammalian ova, but who would say that a chorion was essential in the development of a dermoid cyst?

The discussion was continued at a special meeting held on June 16th, under the presidency of Dr. Malins.

Dr. Galabin said that he had from the first been a believer in the view that the so-called deciduoma malignum was the result of pregnancy, and that it was a fœtal epithelioma implanted upon the mother. He had listened, therefore, with great satisfaction to the convincing demonstration which Dr. Teacher had given of both these propositions.

He had been himself convinced by the relation, not so much to pregnancy as to vesicular mole. While pregnancy was common the frequency of vesicular mole was estimated as only about one in 2,000 pregnancies. Not more, therefore, than about one woman in every 20,000 at the most would have had at any given time a vesicular mole within a year. But in deciduoma malignum vesicular mole was the antecedent in something like half the cases, and this proportion had been maintained from the earliest record up to the present. It was possible on this basis to calculate by the mathematical theory of probabilities what was the chance against the vesicular mole having occurred within a year before half of the cases of deciduoma malignum, if there was no causal relation between them. The result was that the probability increased very rapidly as the

number of cases increased. Within eight or ten cases a probability of a million to one was reached, and when the cases amounted to 40 or 50 the probability was an unimaginable number of billions of billions to one.

He contended that there was already, at the time of the discussion in the Society in 1896, ample demonstration that there was a causal relation between vesicular mole and deciduoma malignum; since out of 40 cases then recorded, vesicular mole had preceded in 18.

When the number recorded had reached 90 the number preceded by vesicular mole was 49. The relation to pregnancy in general would hardly be denied if that to vesicular mole were admitted, especially since the disease more often followed an abortion than a full term pregnancy. He was surprised, therefore, that, at the former debate, Dr. Spencer was the only speaker who argued decidedly in favour of the connection.

The existence of a similar structure in some cases of sarcoma of the testis was then quoted as an objection to deciduoma malignum being a result of pregnancy. But if such a structure were found only in tumours classed as embryomata, from their resemblance to the imperfect development of an ovum, he thought that this was not an objection but an argument in favour of deciduoma malignum in the uterus being derived from a fertilized ovum.

He did not consider that embryomata were derived from an included ovum the brother or sister of the individual who bore it. Such a brother ovum was generally attached on the surface, and there was no reason why it should be in the testis or ovary rather than elsewhere. He thought that they were instances of imperfect parthenogenesis or attempt at development of germ plasm without union of the sexes. The germ plasm was supposed to be nominally concentrated in the testis and ovary and, therefore, such tumours generally occurred there. But it was conceivable that there might be some aberrant fragment of it in such a situation as the mediastinum.

Even if a structure resembling deciduoma malignum were found in other parts of the body this would be no argument against its specificity in the uterus, or its being the result of pregnancy there unless it could be shown that in the uterus deciduoma malignum occurred quite outside the age of possible pregnancy. Since malignant disease of the body of the uterus was much commoner after the menopause than before, deciduoma malignum, if it were an ordinary tumour, should be found long after the menopause. But, on the contrary, the average age for it was 31, just the middle of the period of fertility. Although cases had been recorded up to the age of 55, and as much as two years after the menopause, this was obviously no proof that they were not the result of pregnancy since the disease might be latent for a time.

It was a further step to show that the tumour was a chorionepithelioma. The chief proofs were the continued vitality of villi after death of the embryo, as shown at the last meeting by a section of ovum retained five months in the uterus; the identity of appearance of the syncytium and the cell masses of deciduoma malignum, with the syncytium and cell masses seen in early pregnancy, and especially in vesicular mole; the continuity of the syncytium with the syncytium of the villi when villi were present in the tumour, and the few cases recorded in which actual villi were present, not only on the primary growth, but in metastases. He had shown at the last meeting a section of vesicular mole, with cell masses as well as syncytium, resembling those of deciduoma malignum. The same was shown still better in the beautifully stained sections exhibited

by Dr. Stevens, one from Dr. Galabin's case of deciduoma malignum. The size and appearance of the cells, their nuclei, and the karyokinetic figures in them were identical.

He did not, however, think it advisable to change the name since, if a name were in general use, it did not matter much that its derivation was erroneous. No one wanted to change the names of decidua reflexa or decidua serotina. In the term of deciduoma malignum had been comprised a definite clinical group of tumours, characterised not only by their causation, but by their high malignancy and tendency to form metastases, both in the neighbourhood and in the viscera, and to lead to extensive necrosis and formation of blood spaces. Some few of these showed only cells and no syncytium, and had the appearance of sarcoma. They were, therefore, certainly not syncytioma, and it was difficult to show them to be chorion-epithelioma, although he believed that they might be such in their origin.

He did not think that Dr. Teacher's figures showed so conclusively that the cell masses of the tumour were directly derived from the Langhans' layer of the villi. The point could best be studied in vesicular mole, which showed similar cell masses. If these were so derived, the first step ought to be the formation of a cluster of cells covered in a cap of syncytium. He had occasionally seen this, but more often the cell masses appeared to be separated from the villus by the syncytium. If the syncytium and Langhans' layer were both modifications of the fœtal epiblast it seemed probable that one might be converted into the other, and that syncytium might become differentiated into cells. Intermediate appearances might be seen, both in vesicular mole and in deciduoma malignum.

He thought that the form of deciduoma malignum, in which only cells and no syncytium were seen, and which resembled sarcoma, might be an ultimate development of the more common form.

It seemed chiefly to be found in advanced cases, in which the patient died from the disease without operation. This was so in a case mentioned at the last meeting, and in the case which was at first under his care a a section from which was shown by Dr. Horrocks. Dr. Teacher had pointed out that neither cell masses nor syncytium showed any intercellular substance or vessels. But in the infecting border of the growth very small groups of cells could be seen springing up in the midst of the stroma, and small fragments of syncytium, and these might be reduced to single cells, so that the general appearance resembled sarcoma. Thus if necrosis occurred, of the original cell masses and syncytium, only a sarcomatous looking structure might be left. It would be of interest to know from those who had worked at cancer parasites whether the bodies regarded as parasites were found or not in deciduoma malignum. It was presumed that the only parasitism in the disease was that of the fœtal structures upon the mother, but it was not impossible that microbic parasites might infect the placenta. The elucidation of this point would be of value in the investigations of the origin of cancer in general.

Dr. Herbert Spencer wished to add his thanks to Dr. Teacher for the admirable demonstration, one of the best which had been given before the Society. He thought that Dr. Teacher had in his paper scarcely done justice to the London gynæcologists; it was in London, at University College Hospital, that the first case of deciduoma in this country had been observed (in 1889), and it was at the Obstetrical Society of London that

the first case was published (in 1895). It was also the discussion on that case and two others at the Obstetrical Society, in 1896, that first aroused general interest in this remarkable disease in the United Kingdom.

Dr. Teacher would find that many cases of the disease had been observed in London during the last few years, though they had not all been published, and when published, not always under the same name. A great deal too much attention had been devoted to the name. For his own part, he preferred the name given by Karg to Sänger's case—deciduoma malignum; the object of a name was to act as a label, and not as a definition, and deciduoma malignum served the purpose of a distinctive label sufficiently well. He thought there was some inconsistency in Dr. Teacher's deprecating the inclusion of the disease in the classes of sarcoma and then calling it "chorionepithelioma."

Dr. Spencer thought the chief merit of the discovery of this disease belonged to Chiari rather than to Sänger. It was in any case owing to Chiari's publication (1877) and the report of his cases in Ruge and Veit's *Der Krebs der Gebärmütter* that his own attention had been drawn to the remarkable occurrence of "cancer" of the body of the uterus after labour in young women of 23 and 24 years of age, and that he had been led to investigate the case alluded to above.

With regard to the pathogeny of the disease, he thought it was absolutely established that it arose from the epithelial covering of the chorionic villi. In the discussion at the Society in 1896 (*Obst. Trans.*, 1896, p. 181), he had opposed the views of Drs. Kanthack and Eden, and had given evidence that the disease originated in the products of conception, and in the *Quarterly Medical Journal* for July, 1896, he had written a paper giving the principal facts of forty cases of deciduoma malignum, and he regretted that these facts had not been allowed to prevail against the theories of the critics. He had on those occasions drawn attention, amongst other points, to the striking fact that in at least 45 per cent. of cases the disease followed a hydatidiform mole, which itself shows overgrowth of its epithelial covering, and had alluded to Apfelstedt and Aschoff's case as proving, if the evidence were corroborated, the origin of the growth from chorionic villi. The corroboration had been forthcoming in several cases published since that date, which, in his opinion, clearly proved that these growths arise from the epithelial covering of the chorionic villi. The excellent demonstration given by Dr. Teacher would help to promulgate that view. There was one difficulty which he did not think the demonstration met satisfactorily—namely, the difficulty of distinguishing between an ordinary sarcoma and a deciduoma malignum in cases which contained no syncytium.

With regard to the structures resembling "chorionepithelioma" met with in teratomata, he had not seen a specimen, and would prefer to wait before expressing an opinion. It did, however, appear strange that chorionic villi or the epithelium of the villi, or only structures which developed into chorionic villi, should be "included" in the body of a fœtus.

Dr. Eden said that he wished to express his high appreciation of the splendid demonstration that Dr. Teacher had given at the last meeting upon this subject, and his pleasure at having had the opportunity of introducing Dr. Teacher to the Society.

He had observed that several of the preceding speakers had taken occasion to deprecate the trend of the 1896 discussion upon deciduoma malignum, and to dissociate themselves from the decision which had been

reached, he would not say by the Society, but by the special Committee appointed to investigate the cases laid before the Society upon that occasion. For his own part, he avowed himself an unrepentant sinner, in so far as that discussion and report were concerned, and he reminded Dr. Spencer that, although he (Dr. Spencer) had just told them that he had always believed in the fœtal theory of deciduoma malignum, yet he had signed the report of the Committee, which stated that the cases were sarcomata. After reading once more the reports of the discussion and the papers laid before the Society in 1896, he really believed that, in view of the facts then before them, the decision of the special Committee was a wise one, and under the same circumstances he would be prepared again to take up the same position. It must be remembered that at that time the position of this great question was very different from to-day. He might briefly indicate the then position as follows: Firstly, there was no doubt that in their broad general characters the cases recorded at that time bore a close resemblance to sarcomata, viz., in their age incidence, in their dissemination by venous channels, in the total absence of lymphatic invasion, and microscopically in the absence of connective tissue stroma and vessels, and the presence of masses of multinucleated protoplasm resembling giant cells; secondly, the clinical evidence of connection with pregnancy was in a considerable proportion of the then recorded cases unsatisfactory; thirdly, the theory of Marchand as to the identity in microscopic character, of the tumour elements with those of the chorionic epithelium was new, and unsupported by independent evidence; fourthly, the actual demonstration of the development of the tumour from chorionic villi had not been forthcoming, indeed it was open to doubt whether villi had then been proved to occur in these tumours at all; and, lastly, syncytial elements, then believed to be the essential elements of the tumour, were shown to occur in the male subject, where origin from chorionic epithelium was out of the question. Under these circumstances, he considered that the Committee could have come to no other conclusion, and had nothing to regret with regard to the 1896 discussion.

Having said that, however, he was quite prepared to admit that the course of events had shown that the decision then arrived at was wrong. In the short paper he had read to the Society in 1896 he had indicated that in his opinion the theory of Marchand could only be satisfactorily proved by demonstrating the actual development of the tumour from structures definitely recognisable as placental relics. That condition, he admitted, had since been amply met by a number of cases, and the importance of this point could not be too much emphasised, for all other considerations were subordinate to it. The new growth, having been definitely traced back to the normal tissues from which it arose, its origin must be regarded as settled. But the position since 1896 had changed in other respects, all of which lent support to this view. A large body of expert pathological opinion had grown up in support of the theory of Marchand, which Fellows of that Society, most of whom were not pathological experts, could not question. Again the puzzling class of cases in which the primary disease occurred in the vagina, the uterus being free from disease—cases which had been a serious stumbling block to them in 1896—had now received adequate explanation. Schmorl and Veit had shown that normal villi and fragments of chorionic epithelium could be deported by the blood-stream to distant parts, and there either become absorbed or possibly undergo malignant changes, resulting in the development of disease in remote organs. This interesting class of cases was now

a large one, and instances had been reported where chorionepithelioma had occurred in the vagina, labium majus, tube and ovary, lungs and brain, the uterus in each case being free from disease.

It was therefore evident that the difficulties present in 1896 had now been removed. It was worth while for the Fellows to remember that, although the decision of the 1896 Committee had been erroneous, yet in regard to two important matters, suggestions made in that discussion had actually now received general acceptance. In the short paper, which he (Dr. Eden) had then read, he had expressed the opinion that the syncytial and cellular elements in deciduoma malignum had the same origin, the syncytial masses being formed by degeneration and fusion of the cellular elements. This view was now accepted. And not only so, but Peters had shown that in the human ovum the physiological prototype of these elements bore precisely the same relation to one another; the chorionic epithelium was at first entirely cellular, but on the cells coming in contact with the maternal blood, degeneration and fusion of cells occurred, producing what we called the plasmodial or syncytial layer.

In yet another respect the 1896 discussion had made an important contribution to the subject, and that was in pointing out the fact that syncytial masses similar to those found in deciduoma malignum occurred in malignant testicular growths, whose origin from placental relics was out of the question. This fact had recently been re-discovered by Schlagenhaufer, and had caused a great deal of perturbation in the minds of their German colleagues. Schlagenhaufer's case was clearly a teratoma, while Kanthack had regarded the specimen shown to the Society in 1896, as a sarcoma. It was a mystery to him why this observation of Schlagenhaufer's should be regarded as in any way affecting the validity of Marchand's theory of chorionepithelioma; that theory rested upon actual demonstration of the histogenetic origin of the growth, and no such observations as Schlagenhaufer's could upset it. Yet this latter authority had proposed that we should regard as teratomatous, *i.e.*, as due to the "inclusion" of an ovum, a large proportion of the accepted cases of chorionepithelioma in the uterus and elsewhere. Ths appeared to him (Dr. Eden) to throw the subject into needless confusion, for the "inclusion" theory was not required to account for chorionepithelioma, unless cases should ever be proved to occur under circumstances in which pregnancy could be scientifically excluded.

In conclusion, he said that it appeared to him that the pathogenesis of this growth, having been satisfactorily settled, the only questions remaining were clinical questions. For instance, we were quite unable to explain why these growths varied so greatly in malignancy, why those cases in which villi were found in the tumour should be less malignant than others, why cases where the primary growth was in the vagina were less malignant than the uterine cases, why metastases should disappear after removal of the primary growth alone, and, lastly, why in one remarkable case recently recorded by Fleischmann, partial removal of the primary growth should be followed by disappearance of the remainder and complete recovery.

Dr. McCann said he ventured to join in the discussion because he had had three cases of "deciduoma malignum" under his care during a comparatively short space of time.

(Two of these cases will be found fully reported on p. 80 et seq.)

The third patient was aged 53 years, and had ceased menstruating for

18 months. This case had already been fully reported in the *Journal of Obstetrics and Gynæcology of the British Empire* for March, 1903. The uterus was removed by vaginal hysterectomy, and its cavity was found to be completely filled with blood and clot. Her last pregnancy terminated nine years previously at the third month. She was admitted to the Samaritan Hospital in March, 1902.

These three cases demonstrated three distinct clinical types of uterine new growth. In the first case the growth was polypoid and circumscribed; in the second, it was diffused through the uterine mucosa, and in the third the uterine cavity was entirely occupied by blood clots. The last type had been described under the terms angio-sarcoma, cavernous sarcoma and sarcoma teleangiectodes. Dr. McCann thought that in the future such cases would be shown to be of the nature of "deciduoma malignum." They seemed, moreover, to be of comparative rarity.

The description of specimens where the diseases had been actually shown to originate from the coverings of the chorionic villi had completely revolutionised our ideas as to the etiology. For those cases where the occurrence of a previous pregnancy was difficult to prove, the theory that "fœtal relics" had persisted *in utero* seemed to be a fitting explanation. The rarity of the disease appeared to have been exaggerated, for no less than six cases had been observed at the Samaritan Hospital during a comparatively short period.

The degree of malignancy appeared also to vary in different cases. Although it was true that some types are especially malignant, there are others in which this character is not so well marked. In all probability the polypoid or circumscribed type was the least malignant, thus resembling polypoid sarcomata of the uterine mucosa.

It it were proved that the secondary growths did disappear then we were justified in dealing surgically with cases in which secondary nodules existed in the vagina, unless the general condition of the patient contra-indicated any operative interference.

Dr. McCann did not think that an adequate explanation had been found for all the cases grouped under the title of "deciduoma malignum," but in attempting to solve the question he advocated careful and accurate records of cases without having in view the support of a particular theory as to the causation of the disease.

Dr. Lockyer said he was glad to have the opportunity of saying how very thoroughly he appreciated listening to Dr. Teacher's most able paper, and of expressing the pleasure it gave him to follow his admirable demonstration. He felt that the Obstetrical Society of London owed Dr. Teacher a debt of gratitude for the infinite pains he had taken in demonstrating his work in the study of chorio-epithelioma. The obligation was the more emphasised by the fact that Dr. Teacher was a visitor, and had spared no labour and expense in the preparation of his instructive demonstration. It was no small satisfaction to Dr. Lockyer to find that his own interpretation of the nature of the growth which has passed under the name of "deciduoma malignum," coincided with Dr. Teacher's views.

In January, 1902, Dr. Lockyer read a paper before this society on "A case of Chorio-epithelioma with Pulmonary Metastases," and by a series of lantern slides he traced the origin of the syncytial masses and Langhans' cells back to the walls of the chorionic villi, and endeavoured to point out that if we accept the fœtal trophoblast as the precursor of Langhans' layer

of the syncytium the term "deciduoma" is a misnomer for a growth containing these elements in its composition.

For such growths a name should be chosen which will indicate their true origin; and after careful study of eight specimens of this disease Dr. Lockyer chose the term of chorio-epithelioma for his two published cases as being the most fitting nomenclature for this purpose. Dr. Teacher had gone further than Dr. Lockyer was formerly prepared to go by concluding that every so-called deciduoma malignum was a chorio-epithelioma. Dr. Lockyer had stated that his experience led him to the conclusion that there were cases in which the histological features differed in essential details from chorio-epithelioma. The specimens which led Dr. Lockyer to this conclusion were prepared by Mr. Corrie Keep, who kindly allowed him to make drawings from them which were shown at the demonstration in January, 1902. He had again examined these specimens, and with his now larger experience in the study of these growths, obtained from the examination of five more specimens since his paper was written, he had no hesitation in saying that although syncytium was not well represented, the cells described by him as "modified connective-tissue cells like those found in normal decidual membrane" were in reality derivatives of Langhans' layer.

In accord with this conviction these growths fell into the category of chorio-epithelioma in spite of the fact that no definite syncytium was present. In other words, syncytium was not the leading feature of these tumours. Sänger's original sarcoma deciduo-cellulare had been shown at this Society by Dr. Teacher. It was a typical chorio-epithelioma, as proved by the presence of both syncytial masses and Langhans' cells.

The only distinction which Dr. Lockyer was at the present time prepared to insist on as existing between these growths was that they contained syncytial derivatives and Langhans' cells, whereas others contained Langhans' cells, while the presence of syncytium was difficult or impossible to prove. His previously expressed opinion that some of these growths could be referred to the maternal decidua he now regards as a point which still requires demonstration, but which may for the present be left an open question.

In the discussion on Dr. Lockyer's paper Dr. Horrocks asked the question, "Could Dr. Lockyer say that in all cases of this malignant growth which had followed vesicular mole, there had been syncytial elements?" As far as his experience went Dr. Lockyer answered this question in the affirmative. Four of the eight cases known to him and in which he found syncytium followed vesicular disease of the chorion. Dr. Horrocks' own specimen proved this point. Dr. Lockyer had examined it carefully and found abundant evidence of the syncytium being represented, so that his statement that "the malignant sequela of a vesicular mole is invariably a syncytioma" needed no alteration. He wished, however, to again emphasise the fact that syncytium was not the essential feature of a chorio-epithelioma as Dr. Horrocks seemed to think.

Whilst leaving the lecturer to discuss the adverse criticisms on his paper, Dr. Lockyer felt it was incumbent upon him to mention that he had himself made a drawing of Dr. Haultain's specimen some two years ago, and was prepared to vouch for the faithfulness of the picture drawn from the same specimen by Dr. Teacher's German artist.

A short abstract of the case shown by Dr. Lockyer at this meeting of the Society was as follows:—

Mrs. V., aged 28, twice pregnant. The first pregnancy ended in the

expulsion of a hydatidiform mole; the second ended in the birth of a healthy child at term. One month after the child was born the mother developed a swelling in the right labium majus and another in the inguinal glands; subsequently another deposit was found in the vagina. The external growths were opened under the impression that they were pyæmic, but only blood clot and necrosed tissue came away.

Death occurred eleven weeks after confinement. The symptoms and course of the disease during the patient's stay of seven weeks in the Hospital for Women at Brighton were mainly those of septicæmia, signs of pulmonary consolidation supervened only a fortnight before death. The primary growth was confined to the body of the uterus; the uterine walls were not perforated, the adnexa were healthy, *there was on infiltration of the parametrium such as was found in uterine sarcomata.* There were secondary growths in the lungs, pancreas, kidney, and vagina. The primary tumour and all the secondary deposits showed syncytial derivatives and Langhans' cells, the syncytium being most abundant in the pancreatic metastases.

Dr. H. Russell Andrews showed two specimens of chorionepithelioma. The first was an old specimen which had been in the museum of the London Hospital for many years labelled "cancer of the uterus." Microscopical examination proved it to be a chorionepithelioma. The second was shown before the Society in 1886 by Dr. Lewers as a specimen of circumscribed sarcoma of the uterus with secondary deposits in the vagina and lungs. Dr. Lewers had kindly allowed Dr. Andrews to redescribe it. Sections showed typical chorionepitheliomatous structure. He commented on the fact mentioned by Dr. Haultain that in some cases the growth seemed to be killed by coagulation of the blood round it, and said that in the majority of cases the extreme malignancy and rapid development of metastases was due to the fact that although the growth always occurred in blood-vessels it did not cause thrombosis. This was probably to be explained by the presence of syncytium, which seemed to have, with endothelium, the property of not coagulating blood with which it was in contact. Although in some sarcomata, especially in those which were sometimes called peritheliomata, cells were often seen, which resemble syncytium, yet the vacuolation, which was so characteristic of chorionepithelioma, was not seen in them.

The complete absence of vessels in chorio-epithelioma was also an important point in distinguishing these tumours from sarcomata in which vessels, although often ill-formed, could always be found.

Dr. Hebb said that in the one case which had passed through his hands, while the general aspect was that of poly-cellular sarcoma, there were appearances reminiscent of epithelial cancers.

The microsections exhibited certain histological features which had not been alluded to by previous speakers; these were attempts, sometimes apparently successful at the formation of new blood-vessels, the existence of irregular mitoses, and the presence of cell-inclusions or "cancer-bodies," the last two being of common occurrence in carcinomata.

He thought that eventually it would be demonstrated that the maternal and fœtal structures participated as to the site of origin of these growths, sometimes the one, sometimes the other location having the greater share.

Dr. Teacher, in reply, thanked the Society for the exceedingly kind manner in which his paper and demonstration had been received. The

keen interest manifested by Fellows in the discussion of the subject had been most gratifying.

The results also were very pleasing to him inasmuch as the views which he had put before the Society appeared to have met with very general approval. In fact, the remarks of various speakers, and especially the summing up of Dr. Eden, left very little in the way of criticism for him to answer. Dr. Teacher felt himself bound to express his approval of the "unrepentant sinner" attitude of Dr. Eden in defending the "decision" of the Society in 1896. The discussion on that occasion was a good one, and the conclusions arrived at were most natural under the circumstances, having in view the material before the Society. Dr. Teacher's criticism of that discussion had been written without knowledge of the fact stated by Dr. Eden, that only the preliminary notice of the case of Apfelstedt and Aschoff was before the meeting of 1896. At the same time, even admitting that, Dr. Teacher adhered to his opinion that the Society had hardly appreciated the strength of the case which Marchand had worked up from the histological resemblances of the tumour and the pathology of hydatidiform mole, and that it was a pity they had delayed the consideration of the new evidence for so long. But there had been one advantage in that delay. The case which had been brought before the Society by the late Professor Kanthack was at that time absolutely inexplicable, and he did not wonder at the influence which it had exercised over the minds of the members of the Pathological Committee. He had always felt a doubt as to the right of Prof. Kanthack to describe such a curious tumour off hand as a sarcoma, but owing to the unfortunate circumstances (namely, the early death of Prof. Kanthack) the materials for a criticism of his view were wanting until the rediscovery of this kind of tumour by Schlagenhaufer. Doubtless, the members of the Society would say that there was not yet a satisfactory explanation of this tumour of the testis, but he thought that they must grant that it was no longer justifiable to call it sarcoma, and also that it could not be held, in the face of the other evidence we now possessed, to effect the specificity of the ordinary chorionepitheliomata.

Dr. Teacher briefly reviewed the various interpretations which were now being offered of those embryomata (or whatever they might be called), the relative merits of which he felt must be left for future consideration.

In reply to the question whether placenta had ever been found in an undoubted teratoma, Dr. Teacher quoted the case of Maydl. Laparotomy in an anæmic but well-developed man of 19 years revealed a tumour lying between two folds of the root of the mesentery. It consisted of a well formed trunk and limbs without a head, but in place of it a long tuft of hair. This imperfect fœtus was enclosed in an amniotic sac; a thickening of the amnion connected with the superior mesenteric artery showed the histological structure of placenta. There was also a case in a sheep described by Rathke in 1830 in which a female fœtus was attached to the head of a male fœtus by an umbilical cord, which passed into the skull and ended in a well-formed placenta growing in the dura mater.

Turning to certain points raised, Dr. Teacher admitted that limitations of time had caused his opening statement to contain more of assertions than of proof, but, on the other hand, the critics who had raised that objection seemed to have failed to follow the demonstration of the relationship of the normal placenta and chorionepithelioma through the simple hydatidiform mole and malignant mole, the series of slides comprising which could hardly have been made more complete.

He also protested against the questioning by two of his critics of the value of evidence simply and solely because it had been "made in Germany." His experience of our German colleagues was that they were a most kind, courteous lot of gentlemen, and as keen and conscientious seekers after truth as any men. In his enquiries he had encroached freely upon their time, and they had given it to him ungrudingly. The race doubtless was no more free than any other from inaccurate and unreliable members, but his own observations had led him to the opinion that the latter got their deserts as surely and swiftly in Germany as anywhere else.

The assertion that the view of Veit remained purely hypothetical was based upon the fact that Dr. Teacher in December, 1902, asked Prof. Veit if a case had yet been found which demonstrated the sequence of events which it supposed. He understood Prof. Veit's reply to be negative. On the other hand, in the 188 cases summarised the presence of villi was noted in 35. A number of these were old malignant moles, not examined microscopically, but there remained a large number of cases in which the origin of the tumour from the chorionic epithelium had been directly demonstrated. Twenty-eight of the cases (including the malignant moles 11 in number) followed molar pregnancy, four abortion, and one (Langhans' No. 2) delivery at term.

That the cases in which villi were found (excluding malignant moles) showed a relatively low degree of malignancy was a fact; he could not explain it. The matter was considered in the paper.

Dr. Fothergill spoke of many cases in which the connection with pregnancy appeared to be absent. Excluding the tubal cases, there remained 181 which Dr. Teacher had synopsized. In 16 of these the occurrence of a preceding pregnancy was not clear from the history. In two of these villi were present; in four cases no history was obtained, either because they were cerebral cases, the nature of which was discovered only at the *autopsy*, or for other valid reason. Of the ten remaining cases nine occurred in women between 24 and 44. Was it possible to exclude pregnancy in those cases? In many cases the disease was continuous with the pregnancy. There were several cases in women of nearly the same age who had not been pregnant for many years, and then developed tumour. In eight out of nine cases over the age of 50 the preceding pregnancy was molar. As an example might be taken the case of Gunther (recently reported by Marchand, a photograph from which was included in Dr. Teacher's demonstration). The patient was 53¼ years old; her last child was born in her 39th year, and then after 13 years she had a hydatidiform mole, which passed on into chorionepithelioma.

An apparent menopause was recorded in two clear cases, besides that of McCann. An explanation, which might apply to all these long interval cases, had been offered by Marchand:—It was well known that portions of epidermis included in the closure of some of the embryonic clefts might lie latent ten or twenty years, or even longer, and then develop into tumours. In view of that he thought there was nothing strange about portions of trophoblast lying latent three or four years and then springing into renewed activity. The hypothesis that those cases might be really of teratomatous nature, Dr. Teacher regarded as quite unnecessary.

Cases of chorionepithelioma without syncytium had been mentioned. There were three cases in which the typical sprawling masses were absent, but none of these could really be said to contain no syncytium, as they all showed syncytial derivatives like the syncytial wandering cells. These cases and the "pure syncytial" cases, all of which actually contained

individual cells, although not typical Langhans' layer cells, Dr. Teacher would regard as varieties of no great importance in view of the relationship which existed between the two layers of the chorionic epithelium. In all of his tumours the relative amount of the different elements varied considerably in different parts of the growth.

With regard to the question of nomenclature, Dr. Teacher said that "syncytioma" was a bad name, because the syncytium was not *the characteristic* element of chorionic epithelioma. The Langhans' layer cells and large individual cells of intermediate type were equally characteristic. Almost any feature of the growth taken by itself could be paralleled from other tumours, but not the combination of features. Lastly, the most characteristic thing was the physiological prototype. He preferred a name which informed one of the source of the tumour, and he thought that the members of the Society need not be afraid of committing themselves to a particular view. He was pleased to find that in this he had the support of Dr. Eden. The most appropriate name therefore was chorionepithelioma, or, if they preferred it, chorio-epithelioma. He was also in favour of allowing the historic deciduoma malignum as a clinical term; it was so well known and so generally used. Moreover the view implied in it was so completely abandoned that the term might be said to have ceased to be misleading. If there were a real "deciduoma" it had not yet been demonstrated; but when so experienced a pathologist as Chiari was inclined to reserve his opinion, Dr. Teacher thought they need not dogmatise; but neither need they "hedge."

Dr. Teacher concluded by again thanking the Society.

NOTE.—Owing to pressure upon our space we are compelled to hold over until the next issue several other Reports of Societies.

REVIEWS OF RECENT BOOKS.

Ueber das Chorionepithelioma und die analogen Wucherungen in Hodenteratomen ("On Malignant Chorionepithelioma and the Analogous Proliferations in Teratomata of the Testis"). von Dr. W. Risel, 1 Assistenten am pathologischen Institute zu Leipzig. Leipzig: S. Hirzel, 1903.

This is a well-illustrated monograph of 170 pages, containing a *resumé* of the literature and full accounts of several hitherto unpublished cases.

The first part of the work is devoted to chorionepithelioma. After a review of the more recent literature on this subject the author discusses chorionepithelioma in general, hydatidiform mole and its relation to chorionepithelioma, and the evidence in favour of the view that the malignant tumour arises from the chorionic epithelium. He goes on to discuss cases where metastatic deposits of chorionepithelioma have been found without malignant growth in the uterus or tubes. He then considers the theories that have been brought forward regarding the causation of the malignant proliferation in chorionepithelioma. He gives a short *resumé* of the accounts given of chorionepithelioma in recent editions of text-books (German only). Here there is much less unanimity of opinion than in recent German papers and monographs. Risel criticises most of the writers of recent German text-books on midwifery and gynæcology. Some of them still write of "deciduoma malignum," some of "syncytioma," etc., and they have not all adopted the true faith as regards the origin of the syncytium. Ziegler, for instance, in the 1902 edition of his well-known work on pathology considers that syncytium is derived from uterine epithelium, and that chorionepithelioma is a carcinoma of the placenta, affecting both the maternal and fœtal parts of it.

The author describes six cases of chorionepithelioma that have come under his own observation. Two of these recovered, one after extirpation of the uterus, the other after removal of the uterus and the vaginal growths. Four of the cases followed hydatidiform mole. One case was a typical chorionepithelioma, in another the connection could be clearly traced between the cells which infiltrated the uterine wall and those covering the vesicles of a mole. The other four cases belonged to atypical or transitional forms of chorionepithelioma. In one of them there was no tumour-formation in the strict sense of the term, rather a dense diffuse infiltration of the uterus with ectodermal cells. In another case there was no trace of tumour formation in the neighbourhood of the placental site, although there were chorionepitheliomatous growths in various organs.

The author next describes two cases which gave rise to suspicion of chorionepithelioma without development of a malignant growth. The first followed removal of a hydatidiform mole, the second followed an abortion. The patient in each case was curetted on account of persistent bleeding. Although microscopical examination in each case showed marked invasion of the uterine muscle by fœtal cells, both patients made an uninterrupted recovery. Risel suggests that possibly in each case the curette removed all the malignant growth.

As regards the division of cases into typical and atypical tumours, Risel says there is no sharp dividing line. From the cases where the tumour

exhibits the characteristic appearance of chorionic epithelium in early pregnancy, all intermediate stages can be traced leading to the atypical cases where the characteristic peculiar structure is absent. In such cases there is no tumour-formation in the strict sense, but a progressive infiltration of the tissues with isolated ectodermal cells quite analogous to the invasion of the chorionic "wandering-cells" into the decidua serotina in cases of hydatidiform mole or in the early stages of the formation of the placenta.

Risel does not consider the evidence convincing which has so far been brought forward of the occurrence of chorionepitheliomata made up only of Langhans' cells or only of syncytium. He thinks that the question as to whether they may occur or not is not of much importance, since the common origin of the two varieties of cells has been proved.

The intravascular development of masses of tissues possessing no vessels and no connective-tissue of its own, together with the side-by-side arrangement of syncytium and Langhans' cells, corresponds exactly to the appearance of chorionic epithelium in early pregnancy.

Although usually classed among carcinomata, chorionepithelioma differs markedly from these tumours. In chorionepithelioma there is no connective-tissue framework in which the epithelial cells are embedded, and the growth has no vessels of its own. It develops lying free in the maternal blood-vessels, and some of its elements penetrate the vessel walls, thus causing the large thrombus-like masses of blood and fibrin which are so characteristic. Again the metatases of chorionepithelioma are formed by way of the blood-vessels, those of carcinoma by way of the lymphatics.

The author gives a short account of Aichel's interesting experiments on bitches. A portion of the pregnant uterine horn was crushed for several minutes by forceps. Changes in the fœtal part of the placenta much resembling those found in hydatidiform mole were produced—viz., dropsical swelling of some of the villi with increase in size and also proliferation of their epithelial cells.

The second half of the monograph deals with chorionepithelioma-like growths in teratomata of the testicle. After a *resumé* of the literature on the subject the author describes two cases that he has examined himself. In the first of these he found tissue very much resembling chorion-epithelioma, but also transition forms between this and other epithelial elements. There were cystic spaces, some lined by epithelium with many goblet cells, others lined by ciliated epithelium, some much resembling the medullary canal in embryonic brain tissue, etc. He considers that the chorionepithelioma-like tissue had not arisen from special rudiments of ovuline membranes, but was only a special variety of the very different ectodermal structures that were present.

His conclusions from his own observations and those of others are as follows:—

1. The occurrence in teratomata, and especially in those of the testicle, of tissue formations which coincide in their characteristics with chorion-epithelioma in women is proved beyond question. Proof of the occurrence of such growth in teratomata of other organs is so far wanting.

2. Evidence has not yet been brought forward of the undoubted observation in teratomata of structures resembling hydatidiform mole which can be traced back to chorionic villi formed in the teratomata.

3. Growths of chorionepitheliomatous character spring from fœtal ecto-derm, and have the same origin as the other ectodermal structures of the teratoma.

4. Up to the present time no evidence has been brought forward in support of the theory that fœtal membranes or their derivatives take any part in the formation of these growths.

In the third part of the monograph the author considers shortly the relation of malignant chorionepithelioma in women to the chorion-epithelioma-like growths in teratomata The presence of these growths in tumours of undoubtedly fœtal origin serves to support the theory that chorionepithelioma in women arises only from fœtal elements. Malignant chorionepithelioma in women and chorionepithelioma-like growths in teratomata ought not to be considered to be identical, but, on account of their absolutely different origin, should be sharply divided from one another. The fact that chorionepithelioma-like growths may occur in teratomata of the testicle does not make it necessary for the views hitherto held as regards the origin of chorionepithelioma to be given up in favour of the theory that it arises from a sort of teratoid material.